Access DB# 140373

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Devong, Dac Examiner # : 69332 Date: 12/16/04
Art Unit: 1711 Phone Number 302-1081 Serial Number: 10/625,033
Mail Box and Bldg/Room Location: 6D71 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Formula of claim 1, from the method of claim 51
Thanks.

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: Usha Shrestha	NA Sequence (#)		STN	56.78
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)	2	Questel/Orbit	
Date Searcher Picked Up: 12/22/04	Bibliographic		Dr.Link	
Date Completed: 12/23/04	Litigation		Lexis/Nexis	
Searcher Prep & Review Time: 30	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time: 200	Other		Other (specify)	

PTO-1590 (8-01)

STIC Search Report
EIC 1700

Scientific & Technical Information Center
USPTO

STIC Database Tracking Number: 140373

TO: Duc Truong **Location: REM 10D71** **Art Unit : 1711** **December 23, 2004** **Case Serial Number: 10/625033**	**From: Usha Shrestha** **Location: EIC 1700** **REMSEN 4B28** **Phone: 571/272-3519** **usha.shrestha@uspto.gov**

Search Notes

Search and Information Resources Administration

STIC Search Results Feedback Form

EIC17000

Questions about the scope or the results of the search? Contact ***the EIC searcher or contact:***

Kathleen Fuller, EIC 1700 Team Leader
571/272-2505 REMSEN 4B28

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1713*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

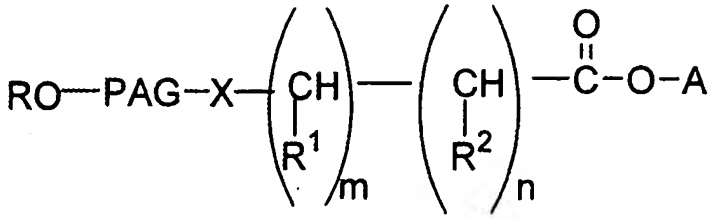
Comments:

Drop off or send completed forms to EIC1700 REMSEN 4B28

10/625,033

WHAT IS CLAIMED IS:

1. A compound of the formula

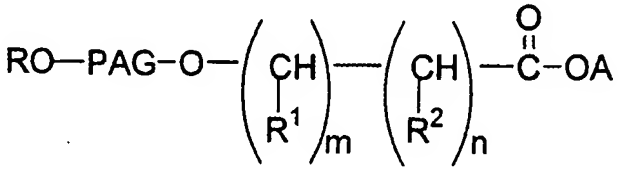


I-A

wherein R, R_1 and R_2 are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons ; n is an integer of from 0 to 1; m is an integer of from 4 to 8; and A is a hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester

or hydrolyzable esters thereof wherein A is hydrogen.

2. The compound of claim 1 having the formula



I-A1

wherein A; R, PAG, R^1, R^2, m and n are as above.

3. The compound of claim 2 wherein A is hydrogen.

45. The compound of claim 42 wherein each PAG^1 residue has a molecular weight of 500 to 15,000.

46. The compound of claim 42 wherein A is a leaving group.

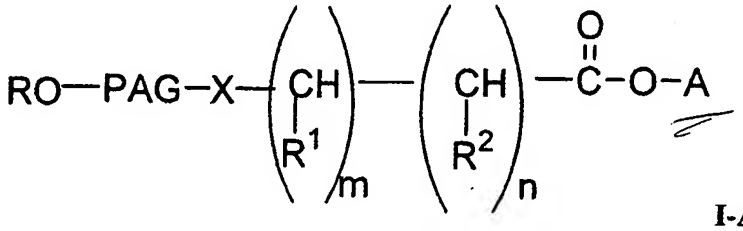
47. The compound of claim 46 wherein said leaving group is N-hydroxysuccinimidyl.

48. The compound of claim 47 wherein PAG^1 is PEG, a divalent polyethylene glycol residue resulting from the removal of both of its terminal hydroxy groups.

49. The compound of claim 48 wherein R is methyl.

50. The compound of claim 49 wherein each PEG residue has a molecular weight of from 500 to 10,000.

51. A process for producing an activated ester of the formula:



I-A

wherein R, R_1 and R_2 are individually hydrogen or lower alkyl; X is -O- or -NH-; PAG is a divalent residue of polyalkylene glycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; n is an integer of from 0 to 1; m is an integer of from 4 to 8; and A is a

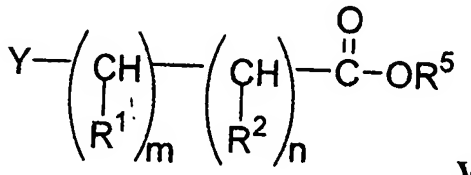
hydrogen or an activated leaving group which when taken together with its attached oxygen atom forms an ester

comprising, condensing a compound of the formula:

V

wherein R, and PAG are as above, and V is -OH or $-NH_2$,

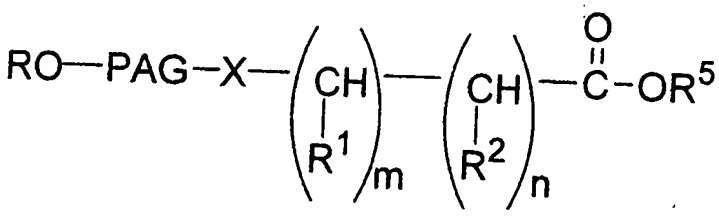
with the compound of the formula:



V1

wherein R^5 forms a hydrolyzable ester protecting group and Y is halide and R^1, R^2, m, and n, are as above,

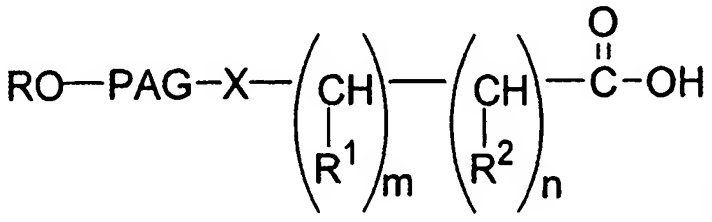
to produce an ester of the formula



VIII

wherein R, PAG, X, R^1, R^2, R^5, m and n are as above,

hydrolyzing said ester to form a free acid of the formula:



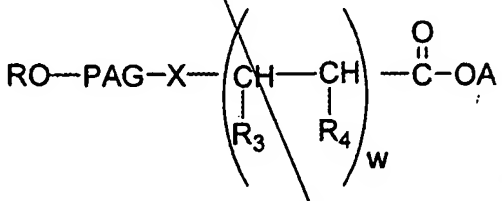
IX

wherein R, PAG, X, R^1, R^2, m and n are as above,

and reacting said free acid with a halide of an activated leaving group in the presence of a coupling agent to produce said activated ester.

52. The process of claim 51 wherein said leaving group is N-hydroxysuccinimidyl group 58.

53. A process for producing an activated ester of the formula:



I-B

wherein R is hydrogen or lower alkyl; X is -O- or-NH-; PAG is a divalent residue of polyalkyleneglycol resulting from removal of both of its terminal hydroxy groups, which residue has a molecular weight of from 1,000 to 50,000 Daltons; w is an integer of from 1 to 3; and one of R_3 and R_4 is lower alkyl and the other is hydrogen or lower alkyl; and A is a hydrogen or an activated

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BIBDATASHEET

Bib Data Sheet

CONFIRMATION NO. 2294

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/625,033	07/22/2003 RULE	528	1711	20917 US1

APPLICANTS

Pascal Sebastian Bailon, Florham Park, NJ;

Chee-Youb Won, Livingston, NJ;

** CONTINUING DATA **********
This appln claims benefit of 60/398,137 07/24/2002

F US 2002-398137/PRV, AP

** FOREIGN APPLICATIONS **********

IF REQUIRED, FOREIGN FILING LICENSE GRANTED
** 02/17/2004

Foreign Priority claimed 35 USC 119 (a-d) conditions met Verified and Acknowledged	☐ yes ☑ no ☐ yes ☑ no ☐ Met after Allowance Examiner's Signature Initials	STATE OR COUNTRY NJ	SHEETS DRAWING 0	TOTAL CLAIMS 67	INDEPENDENT CLAIMS 8

ADDRESS
00151
HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
340 KINGSLAND STREET
NUTLEY , NJ
07110

TITLE
Polyalkylene glycol acid additives

FILING FEE RECEIVED 2016	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

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FILE 'REGISTRY' ENTERED AT 09:57:31 ON 23 DEC 2004
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                ACT DUC625A/A
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L1               STR
L2               SCR 2043
L3   (      12902)SEA SSS FUL L2 AND L1
L4               STR
L5           274 SEA SUB=L3 SSS FUL L4
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     FILE 'HCA' ENTERED AT 08:32:05 ON 23 DEC 2004
L6           441 SEA ABB=ON  PLU=ON  L5
L7            11 SEA ABB=ON  PLU=ON  L6 AND (PAG OR POLYALKYLENE(A)GLYCOL#
                 )
                 D SCAN
L8            13 SEA ABB=ON  PLU=ON  L6 AND (HYDROXYSUCCINIMIDYL OR
                 HYDROXY(A)SUCCINIMIDYL)
L9            23 SEA ABB=ON  PLU=ON  L7 OR L8
                 D SCAN TI
                 D SCAN
L10            0 SEA ABB=ON  PLU=ON  L9 AND COUPLING(A)AGENT#
L11            2 SEA ABB=ON  PLU=ON  L6 AND COUPLING(A)AGENT#
L*** DEL    7804 S L6 AND ACTIVAT?(A)LEAVING(A)GROUP# OR LEAVING(A)GROUP#
L12            0 SEA ABB=ON  PLU=ON  L6 AND (ACTIVAT?(A)LEAVING(A)GROUP#
                 OR LEAVING(A)GROUP#)
                 D SCAN L11
                 D QUE STAT
L13          311 SEA ABB=ON  PLU=ON  L6 AND (PEG OR POLYETHYLENE(A)GLYCOL#
                  OR POLYPROPYLENE(A)GLYCOL# OR PPG OR POLYBUTYLENE(A)GLYC
                 OL OR PBG)
L14            0 SEA ABB=ON  PLU=ON  L6 AND (ACTIVAT?(3A)LEAVING(A)GROUP#
                 OR LEAVING(2A)GROUP#)
L15           10 SEA ABB=ON  PLU=ON  L13 AND (HYDROXYSUCCINIMIDYL OR
                 HYDROXY(A)SUCCINIMIDYL)
L16            8 SEA ABB=ON  PLU=ON  L6 AND (ACTIVAT?(3A)GROUP# OR
                 LEAVING(2A)GROUP#)
                 D SCAN TI
L17            1 SEA ABB=ON  PLU=ON  L13 AND COUPLING(2A)AGENT#
                 D SCAN
L18          311 SEA ABB=ON  PLU=ON  L13(L)(PEG OR POLYETHYLENE(A)GLYCOL#
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```
                                    OR POLYPROPYLENE(A)GLYCOL# OR PPG OR
                  POLYBUTYLENE(A)GLYCOL OR PBG)
L19           99 SEA ABB=ON  PLU=ON  L6(L)(PEG OR POLYETHYLENE(A)GLYCOL#
                  OR POLYPROPYLENE(A)GLYCOL# OR PPG OR POLYBUTYLENE(A)GLYCO
                  L OR PBG)
L20           46 SEA ABB=ON  PLU=ON  L19(L)(PREP/RL)
L21           54 SEA ABB=ON  PLU=ON  L19(L)(PREP/RL OR PREP?)
L22           52 SEA ABB=ON  PLU=ON  L21 NOT L9
L23            1 SEA ABB=ON  PLU=ON  L21 AND (ACTIVAT?(3A)GROUP# OR
                  LEAVING(2A)GROUP#)
L24           81 SEA ABB=ON  PLU=ON  L21 OR L16 OR L15 OR L9
                  SEL L24 RN 1-

=> d que stat
L1                STR
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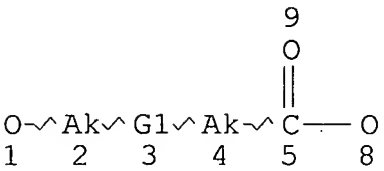


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DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M3-X9 C  AT   4

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NUMBER OF NODES IS   7

STEREO ATTRIBUTES: NONE
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L4                STR
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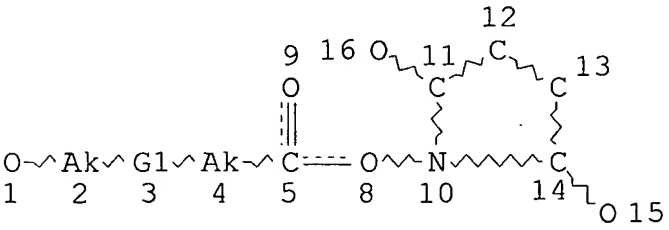


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VAR G1=O/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
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DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M3-X9 C  AT   4

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STEREO ATTRIBUTES: NONE
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L6          441 SEA FILE=HCA ABB=ON  PLU=ON  L5
L7           11 SEA FILE=HCA ABB=ON  PLU=ON  L6 AND (PAG OR POLYALKYLENE(
                A)GLYCOL#)
L8           13 SEA FILE=HCA ABB=ON  PLU=ON  L6 AND (HYDROXYSUCCINIMIDYL
                OR HYDROXY(A)SUCCINIMIDYL)
L9           23 SEA FILE=HCA ABB=ON  PLU=ON  L7 OR L8
L13         311 SEA FILE=HCA ABB=ON  PLU=ON  L6 AND (PEG OR POLYETHYLENE(
                A)GLYCOL# OR POLYPROPYLENE(A)GLYCOL# OR PPG OR POLYBUTYLE
                NE(A)GLYCOL OR PBG)
L15          10 SEA FILE=HCA ABB=ON  PLU=ON  L13 AND (HYDROXYSUCCINIMIDYL
                 OR HYDROXY(A)SUCCINIMIDYL)
L16           8 SEA FILE=HCA ABB=ON  PLU=ON  L6 AND (ACTIVAT?(3A)GROUP#
                OR LEAVING(2A)GROUP#)
L19          99 SEA FILE=HCA ABB=ON  PLU=ON  L6(L)(PEG OR POLYETHYLENE(A)
                GLYCOL# OR POLYPROPYLENE(A)GLYCOL# OR PPG OR POLYBUTYLENE
                (A)GLYCOL OR PBG)
L21          54 SEA FILE=HCA ABB=ON  PLU=ON  L19(L)(PREP/RL OR PREP?)
L24          81 SEA FILE=HCA ABB=ON  PLU=ON  L21 OR L16 OR L15 OR L9


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=> d l24 1-81 ibib abs fhitstr hitind

L24  ANSWER 1 OF 81  HCA  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        141:424601  HCA
TITLE:                   Segmented polymers, their conjugates, and
                         preparation
INVENTOR(S):             Kozlowski, Antoni; Shen, Xiaoming; Bentley,
                         Michael D.; Fang, Zhihao; Sander, Tony L.
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of
                         U.S. Ser. No. 24,357.
                         CODEN: USXXCO
```

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004236015	A1	20041125	US 2003-734858	20031211
US 2002082345	A1	20020627	US 2001-24357	20011218
US 6774180	B2	20040810		
CA 2431977	AA	20020801	CA 2001-2431977	20011218
EP 1345982	A2	20030924	EP 2001-994295	20011218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004525212	T2	20040819	JP 2002-559475	20011218

PRIORITY APPLN. INFO.:		
US 2000-256801P	P	20001218
US 2001-24357	A2	20011218
WO 2001-US49081	W	20011218

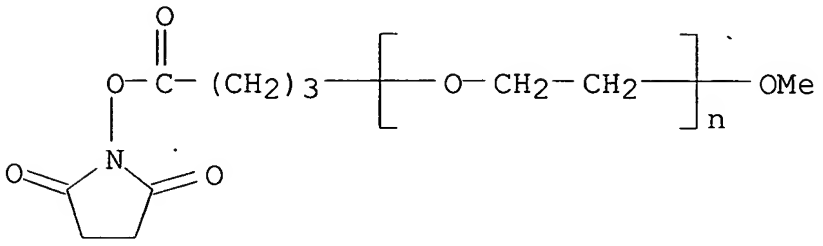
AB Segmented water-soluble polymers contain a higher mol. weight segment linked to a lower mol. weight segment. The polymer segments are poly(ethylene glycol) segments. The segmented polymers are functionalized and are useful intermediates for conjugation to various moieties such as pharmacol. active substances.

IT **187848-51-7P**
(**polyethylene glycol** derivs. for conjugates with biol. active mols.)

RN 187848-51-7 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-

4-oxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM C08G063-48
ICS C08G063-91
NCL 525054200; 525398000; 525399000; 525400000; 525437000; 525535000; 525539000; 525540000
CC 35-8 (Chemistry of Synthetic High Polymers)
IT 9041-92-3DP, reaction product with polyethylene glycol derivs. 32130-27-1P 99126-64-4P 125061-88-3P 174569-25-6P **187848-51-7P** 439590-71-3P
(**polyethylene glycol** derivs. for conjugates with biol. active mols.)

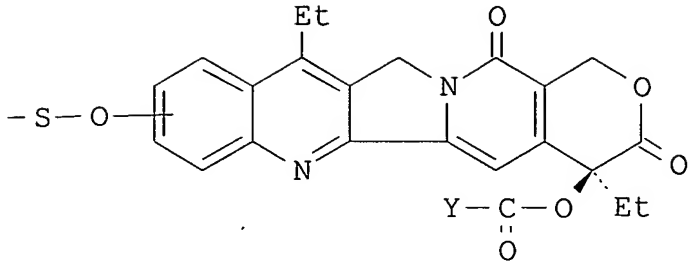
L24 ANSWER 2 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 141:380058 HCA
TITLE: Hydroxy-substituted 20-acyloxycamptothecin polymer derivatives and use of the same for the manufacture of an antiproliferative medicament
PATENT ASSIGNEE(S): Debio Recherche Pharmaceutique S.A., Switz.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004092205	A1	20041028	WO 2003-IB1430	20030416

W: CH

PRIORITY APPLN. INFO.: WO 2003-IB1430 20030416

GI

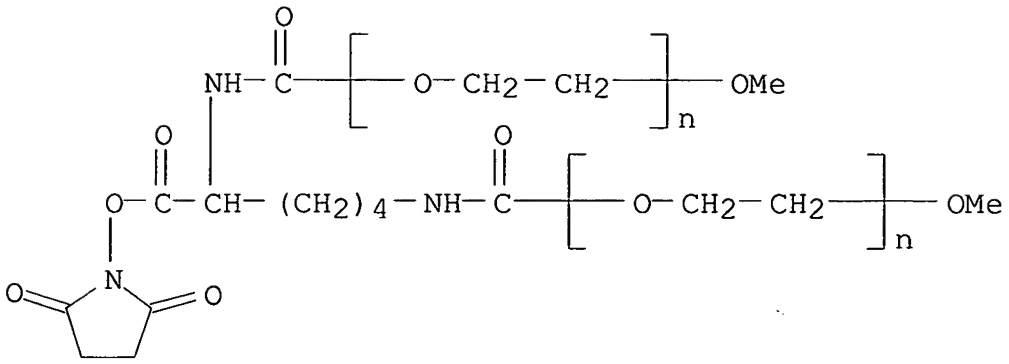
X = 

AB The present invention relates to pharmacol. active hydroxy-substituted 20-acyloxy-7-ethylcamptothecin polymer derivs., X1C(:O)O(CH2CH2O)n(C:O)X2 [I; n = 10 - 1000; when X1 = (un)branched C1-6-alkyl then C(:O) is missing; or X1, X2 = X; Y = Me(CH2)m; m = 1 - 18; S = peptide spacer {e.g., Gly-Leu-Phe-Gly, Gly-Phe-Leu-Gly, Gly-Phe-Phe-Ala, Gly-Phe-Phe-Leu, Gly-Phe-Tyr-Ala, Ala-Gly-Val-Phe, Gly-Leu-Ala, Gly-Leu-Gly, Gly-Phe-Gly, Gly-Phe-Ala, D-Ala-Phe-Lys, D-Val-Leu-Lys, Lys-Gly-Leu-Phe-Gly (with at least one of α- and ε-amino of Lys being linked through a carbamate bond or linked with an aliphatic diamine though a carbamate bond)}], which have antiproliferative cell activity and are water-soluble Thus, H-Gly-Leu-Phe-Gly-OH is treated with 10 kD **polyethylene glycol** monomethyl ether benzotriazolyl carbonate, and then coupled with 7-ethyl-10-hydroxycamptothecin 20-O-propionate to give the tethered alkaloid I [X1 = Me (with no C:O next to it), X2 = X, Y = Et, S = Gly-Leu-Phe-Gly, **PEG** = 10 kD]. The latter was tested for pharmacol. activity [T/C = 130% at 50 mg/kg and 164% at 100 mg/kg in mice injected with P388/VCR cells].

IT **159540-80-4D**, L-Lysine N-**hydroxysuccinimidyl** ester α,ε-bis(**polyethylene glycol** monomethyl ether carbamate), 10 kD **PEG**
(reaction of, with tetrapeptide; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

RN 159540-80-4 HCA

CN Poly(oxy-1,2-ethanediyl), α,α'-[[(1S)-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-1,5-pentanediyl]bis(iminocarbonyl)]bis[.omega.-methoxy- (9CI) (CA INDEX NAME)



IC ICM C07K005-083
ICS C07K005-103; C07K007-06; A61K038-06; A61K038-07; A61K038-08; A61K047-48; A61P035-00

CC 31-5 (Alkaloids)
Section cross-reference(s): 1, 7, 34, 35, 63

IT Polymers, reactions
(**PEG** derivs., alkaloid linkers; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 781640-44-6DP, 10 kD **PEG**
(hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 781640-47-9DP, 10 kD **PEG**
(hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 781640-41-3DP, 10 kD **PEG** 781640-43-5DP, 10 kD **PEG**
(hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 782486-89-9P, 7-Ethyl-10-[(p-nitrophenoxycarbonyl)oxy]camptothecin 20-O-propionate
(preparation and coupling of, with peptide **PEG** derivative; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 782486-81-1P, 7-Ethyl-10-hydroxycamptothecin 20-O-propionate
(preparation and coupling of, with peptide **PEG** derivs.; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 782486-85-5P, 7-Ethyl-10-hydroxycamptothecin 20-O-undecanoate
(preparation and coupling of, with peptide **PEG** derivs.; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 781640-45-7DP, 10 kD **PEG** 782486-79-7P, 7-Ethyl-10-[(tert-butoxycarbonyl)oxy]camptothecin 20-O-propionate

782486-83-3P, 7-Ethyl-10-[(tert-butoxycarbonyl)oxy]camptothecin 20-O-undecanoate
(preparation and deprotection of; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 781640-39-9DP, 10 kD **PEG**
(preparation and enzymic hydrolysis of, with Cathepsin B1; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 781640-40-2DP, 10 kD **PEG**
(preparation and enzymic hydrolysis of, with Cathepsin B1; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 511274-84-3DP, 10 kD **PEG**
(preparation and reaction of, with camptothecin derivative or piperazinecarboxylate; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 511274-86-5DP, 10 kD **PEG** 511274-88-7DP, 10 kD **PEG** 614759-68-1DP, 10 kD **PEG** 781640-46-8DP, 10 kD **PEG**
(preparation and reaction of, with camptothecin derivative; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 782486-91-3, H-Gly-Leu-Phe-Gly-OH hydrochloride 782486-94-6, H-Gly-Leu-Gly-OH hydrochloride
(reaction of, with **PEG** derivative; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

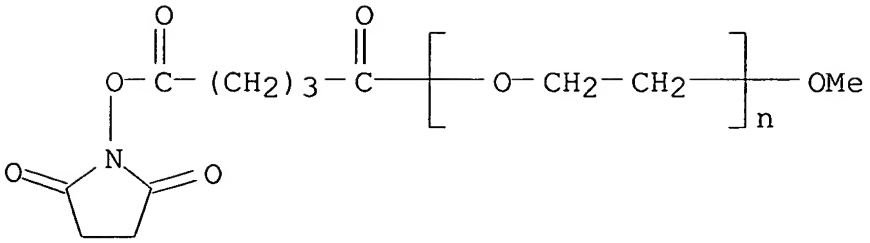
IT 32976-74-2, H-Gly-Leu-Phe-Gly-OH
(reaction of, with **PEG**; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

IT 25322-68-3, **Polyethylene glycol**
159540-80-4D, L-Lysine N-**hydroxysuccinimidyl** ester α,ε-bis(**polyethylene glycol** monomethyl ether carbamate), 10 kD **PEG** 243468-66-8D, **Polyethylene glycol** monomethyl ether N-hydroxybenzotriazolyl carbonate, 10 kD **PEG**
(reaction of, with tetrapeptide; hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 141:230560 HCA

TITLE: Protein carboxyl amidation increases the potential extent of protein polyethylene glycol conjugation
AUTHOR(S): Li, Shukuan; Yang, Zhijian; Sun, Xinghua; Tan, Yuying; Yagi, Shigeo; Hoffman, Robert M.
CORPORATE SOURCE: AntiCancer, Inc., San Diego, CA, 92111, USA
SOURCE: Analytical Biochemistry (2004), 330(2), 264-271
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chemical coupling of polyethylene glycol (PEG) to therapeutic proteins reduces their immunogenicity and prolongs their circulating half-life. The limitation of this approach is the number and distribution of sites on proteins available for PEGylation (the N terminus and the .vepsiln.-amino group of lysines). To increase the extent of PEGylation, we have developed a method to increase the number of PEGylation sites in a model protein, recombinant methionine α,γ-lyase (recombinant methioninase; rMETase), an enzyme cancer therapeutic cloned from Pseudomonas putida. RMETase was first PEGylated with methoxypolyethylene glycol succinimidyl glutarate-5000 with a molar ratio of PEG:rMETase of 15:1. The carboxyl groups of the initially PEGylated protein were then conjugated with diaminobutane, resulting in carboxyl amidation. This reaction was catalyzed by 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide, a water-soluble carbodiimide. The steric hindrance provided by the PEG chains already coupled to the protein prevented crosslinking between rMETase mols. during the carboxyl amidation reaction. The carboxyl-amidated PEGylated rMETase was hyper-PEGylated at a molar ratio of PEG to PEG-rMETase of 60:1. Biochem. anal. indicated that 13 PEG chains were coupled to each subunit of rMETase after hyper-PEGylation compared with 6-8 PEG chains attached to the non-carboxyl-amidated PEG-rMETase. Approx. 15-20% of the non-PEGylated rMETase activity was retained in the hyper-PEGylated mol. Immunogenicity of the hyper-PEG-rMETase was significantly reduced relative to PEG-rMETase and rMETase. Initial results suggested that hyper-PEGylation may become a new strategy for PEGylation of protein biologics.
IT **111575-54-3DP**, reaction products with methioninase and diaminobutane
(protein carboxyl amidation increasing the potential extent of protein **polyethylene glycol** conjugation for drug delivery)
RN 111575-54-3 HCA
CN Poly(oxy-1,2-ethanediyl), α-[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 34
IT 333-93-7DP, 1,4-Diaminobutane dihydrochloride, reaction products with methioninase and PEG derivs. 42616-25-1DP, Methioninase;, reaction products with PEG derivs. and diaminobutane **111575-54-3DP**, reaction products with methioninase and diaminobutane
(protein carboxyl amidation increasing the potential extent of protein **polyethylene glycol** conjugation for drug delivery)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 141:157479 HCA
TITLE: Preparation of peptides and their PEG derivatives by protection of untargeted amine sites
INVENTOR(S): Lee, Sang-deuk; Lee, Kang-choon; Na, Dong-hee; Youn, Yu-seok
PATENT ASSIGNEE(S): Pegsphere Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004065412	A1	20040805	WO 2003-KR118	20030118

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,

NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

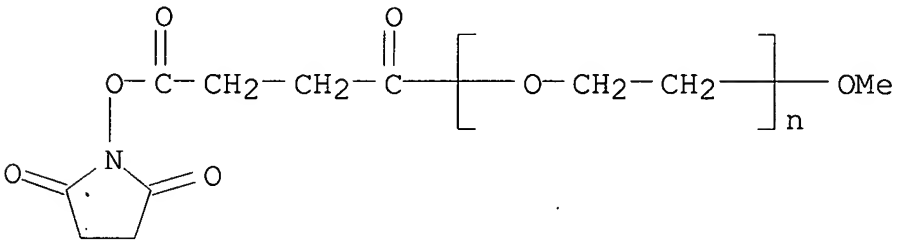
PRIORITY APPLN. INFO.: WO 2003-KR118 200301 18

AB The invention relates to synthetic peptides having selectively protected amines of untargeted sites and to specifically conjugating poly(ethylene glycol) (PEG) to targeted sites of the synthetic peptides. Thus, 1,11-di-Fmoc-protected salmon calcitonin was prepared by the solid-phase method and reacted with PEG and succinimidyl propionate to afford Lys18-PEG 2K-salmon calcitonin, as shown by reverse-phase chromatog.

IT **78274-32-5**
(**preparation** of peptides and their **PEG** derivs. by protection of untargeted amine sites)

RN 78274-32-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM C07K001-06

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 9, 35

IT 47931-85-1, Salmon calcitonin **78274-32-5** 86168-78-7
121559-53-3 123502-58-9 135649-01-3 174569-25-6 286460-84-2
(**preparation** of peptides and their **PEG** derivs. by protection of untargeted amine sites)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 141:145752 HCA
TITLE: Tissue reactive polymer compounds and

compositions for drug delivery

INVENTOR(S): Takacs-Cox, Aniko; Toleikis, Philip M.; Maiti, Arpita; Embree, Leanne

PATENT ASSIGNEE(S): Angiotech International G.m.b.H., Switz.; Gravett, David M.

SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060405	A2	20040722	WO 2003-US41576	20031230
WO 2004060405	C1	20040930		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004219214	A1	20041104	US 2003-749123	20031230

PRIORITY APPLN. INFO.:		
US 2002-437384P	P	20021230
US 2003-440924P	P	20030117

AB A composition comprising a synthetic polymer that contains multiple **activated groups**, and optionally a drug, and method of using such compns. in medical as well in device applications is described. The multiple **activated groups** are reactive with functionality present on animal tissue, so that upon administration of the polymer to the tissue,

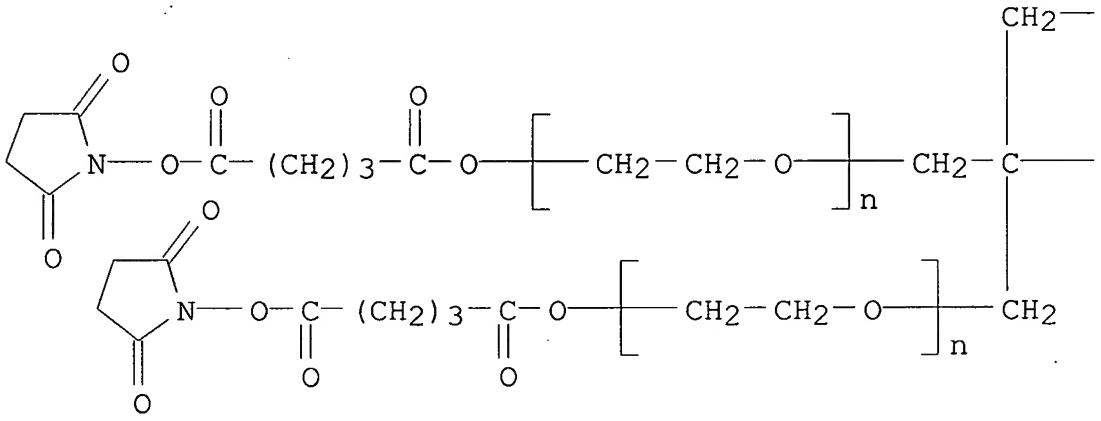
the polymer binds to the tissue. Alternatively, the multiple **activated groups** are reactive with functionality present on a non-living surface, such as the surface of a medical device, where the polymer binds to this surface to, e.g., increase the lubricity of the surface. When drug is present in the composition, the drug is then delivered to the site of polymer attachment. For example, a piece of catheter tubing was dipped into a 1% chitosan solution, allowed to incubate for 10 min, and air dried to obtain a base coat. The chitosan-coated catheter was then immersed into a freshly prepared 10% solution (pH about 8) of tetra functional poly(ethylene glycol) succinimidyl glutarate (4-arm-NHS-PEG) for 5 min. The tubing was removed, rinsed with water and dried.

IT **302781-03-9P**
(preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)

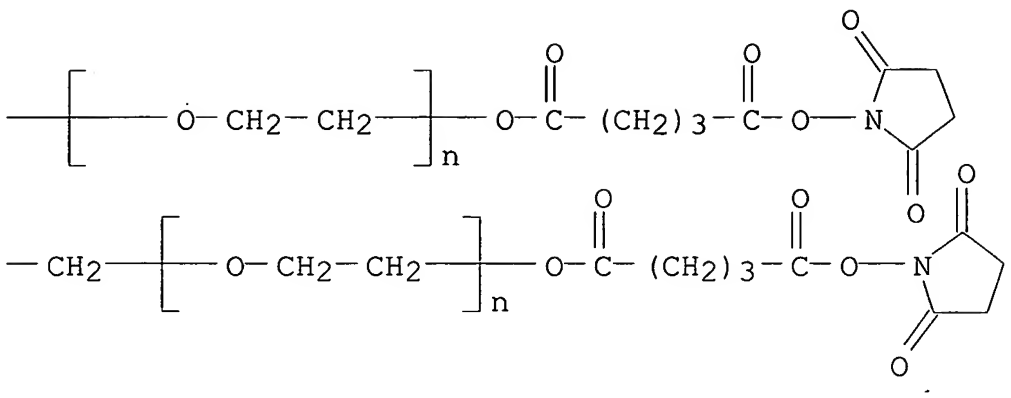
RN 302781-03-9 HCA

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-[[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]oxy]-, ether with 2,2-bis(hydroxymethyl)-1,3-propanediol (4:1) (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IC ICM A61K047-48
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 35
IT Heat-shock proteins
(HSP 90, antagonists; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Transcription factors
(NF-κB (nuclear factor of κ light chain gene enhancer in B-cells), inhibitors; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Estrogen receptors
Peroxisome proliferator-activated receptors
(agonists; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Chemokine receptors
Endothelin receptors
Fibrinogens
Interleukin 1
Interleukin 4
Monocyte chemoattractant protein-1
Retinoic acid receptors
(antagonists; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Macrolides
(antibiotics; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Cytotoxic agents
(antimetabolites; preparation and biomedical uses of surface-reactive
polymers containing multiple **activated groups**)

IT Mammary gland
(artificial, prevention of adhesion related to; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Adhesives
(biol. tissue; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Medical goods
(catheters, coating; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Intestine, neoplasm
(colon, surgery, prevention of adhesion after; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Artery, disease
(coronary, restenosis, prevention of; preparation and biomedical uses
of surface-reactive polymers containing multiple **activated groups**)
IT Polyesters, biological studies
(dilactone-based; preparation and biomedical uses of surface-reactive
polymers containing multiple **activated groups**)
IT Radicals, biological studies
(inhibition of formation of; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Adhesion, biological
Angiogenesis
Cell division
Cell migration
Inflammation
(inhibition of; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Fibrosis
(inhibition; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Cell cycle
(inhibitors; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Vitronectin
(inhibitors; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Mammary gland, neoplasm
(lumpectomy, prevention of adhesion after; preparation and biomedical
uses of surface-reactive polymers containing multiple

activated groups)
IT Antibiotics
(macrolide; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Tumor necrosis factors
(macrophage production of; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Drug delivery systems
(microspheres; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Cytokines
(modulators; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Functional groups
(multiple, reactive; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Drug delivery systems
(nanospheres; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Macrophage
(nitric oxide and TNF-α production by; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Alkylating agents, biological
Angiogenesis inhibitors
Animal tissue
Antihistamines
Buffers
Coating materials
Contact lenses
Cytotoxic agents
Fungicides
Immunomodulators
Leukotriene antagonists
Micelles
Oviduct
(preparation and biomedical uses of surface-reactive polymers containing
multiple **activated groups**)
IT Glycosaminoglycans, biological studies
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
Proteins
Taxanes
(preparation and biomedical uses of surface-reactive polymers containing

multiple **activated groups**)
IT Polymers, biological studies
(reactive-group containing; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Artery, disease
(restenosis, prevention of; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Microtubule
(stabilizing agents; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Abdomen
Blood vessel
Brain
Heart
Liver
Neoplasm
Nose
Pharynx
Spinal cord
(surgery, prevention of adhesion after; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Uterus
(surgical adhesion in, prevention of; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Medical goods
(tissue adhesives; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Liver
(toxicity, surgery, prevention of adhesion after; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Blood plasma
(treatment for; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Surgery
(vascular, prevention of adhesion after; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)
IT Alkaloids, biological studies
(vinca; preparation and biomedical uses of surface-reactive polymers

containing multiple **activated groups**)

IT Integrins
(αIIbβ3, antagonists; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)

IT Transforming growth factors
(β-, inhibitors; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)

IT 10102-43-9, Nitric oxide, biological studies 57576-52-0, Thromboxane A2 122191-40-6, ICE proteinase 167397-96-8, IRAK kinase
(antagonists; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)

IT 9002-98-6, Polyethylenimine 9012-76-4, Chitosan
(base coat; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)

IT 9002-05-5, Factor Xa 9004-06-2, Elastase 9025-82-5, Phosphodiesterase 9028-35-7, HMG-CoA reductase 9028-93-7, Inosine monophosphate dehydrogenase 9029-03-2, Dihydroorotate dehydrogenase 9032-58-0, Farnesyl transferase 9043-29-2, Phospholipase A1 9059-25-0, Lysyl hydroxylase 62031-54-3, Fibroblast growth factor 79079-06-4, EGF receptor tyrosine kinase 80449-02-1, Tyrosine kinase 80619-02-9, 5-Lipoxygenase 101463-26-7 139691-76-2, Raf kinase 141349-86-2, CDK2 kinase 141907-41-7, Matrix metalloprotease 155215-87-5, JNK kinase 165245-96-5, P38 MAP kinase 362516-16-3, IKK 1 kinase 362517-43-9, IKK2 kinase 372092-80-3, Protein kinase
(inhibitors; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)

IT 19542-67-7, BAY 11-7082 65271-80-9, Mitoxantrone
(preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)

IT 51-85-4, Cystamine 112-53-8, Lauryl alcohol 112-76-5, Stearoyl chloride 124-22-1, Lauryl amine 124-30-1, Octadecyl amine 506-30-9, Eicosanoic acid 2156-97-0, Lauryl acrylate 2885-00-9, Octadecyl mercaptan 24991-53-5 60182-11-8, Polyethylene glycol acrylate 60984-57-8, N,N'-Bis(acryloyl) cystamine 76931-93-6, Succinimidyl acetyl thioacetate 83306-17-6 196936-04-6
(preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)

IT 197389-42-7P
(preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)

IT 6162-69-2P 6162-70-5P 9045-69-6P 25322-68-3DP, thiol derivs.

60182-11-8DP, thiol derivs. 76931-93-6DP, ethoxylated derivs.
111600-41-0P 199915-32-7P 228716-21-0P **302781-03-9P**
327155-92-0P 357277-62-4P 693252-88-9P 693815-29-1P
724786-23-6P 724786-24-7P 724786-25-8P 724786-26-9P
724786-27-0P **724786-28-1P 724786-29-2P**
724786-30-5P 724786-31-6P 724786-32-7P
(preparation and biomedical uses of surface-reactive polymers containing
multiple **activated groups**)

IT 50-07-7, Mitomycin C 51-21-8, 5-Fluorouracil 57-22-7, Vincristine 59-05-2, Methotrexate 865-21-4, Vinblastine 2068-78-2, Vincristine sulfate 7689-03-4, Camptothecin 9002-89-5, Polyvinyl alcohol 13598-36-2D, Phosphonic acid, alkylidenebis- derivs. 23214-92-8, Doxorubicin 26780-50-7, Poly(lactide-co-glycolide) 33069-62-4, Paclitaxel 33419-42-0, Etoposide 51110-01-1, Somatostatin 53643-48-4, Vindesine 71486-22-1, Vinorelbine 114977-28-5, Docetaxel 128908-32-7, Melanocortin 151769-16-3, TACE 257939-61-0, Peloruside A
(preparation and biomedical uses of surface-reactive polymers containing
multiple **activated groups**)

IT 9054-75-5, Guanylate cyclase
(stimulants; preparation and biomedical uses of surface-reactive polymers containing multiple **activated groups**)

L24 ANSWER 6 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 141:59651 HCA
TITLE: Preparing antigen masked red blood cells having reduced hemolysis by sera by modification with PEG derivatives
INVENTOR(S): Stassinopoulos, Adonis; Mathur, Shruti
PATENT ASSIGNEE(S): Cerus Corporation, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050897	A2	20040617	WO 2003-US38349	200312 03
WO 2004050897	A3	20040826		

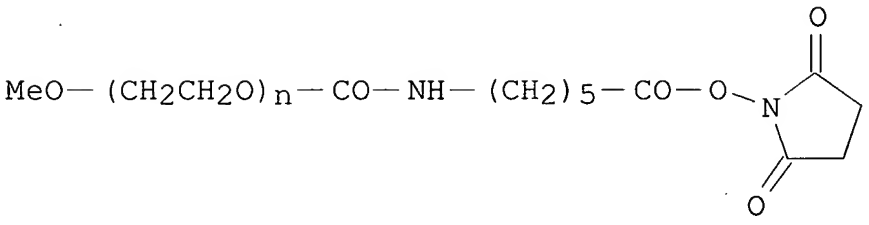
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2002-431213P	P 20021204
US 2002-431214P	P 20021204
US 2002-431215P	P 20021204
US 2002-431216P	P 20021204

GI



I

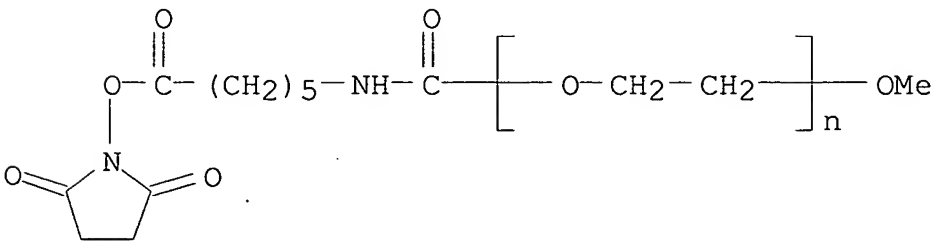
AB Methods are provided for the preparation of an RBC composition having significantly reduced antigenicity and having reduced levels of hemolysis by any serum or plasma sample. The methods of preparation of the red cell compns. involve the reaction of an activated antigen masking compound having a mol. weight of approx. 20-40 kDa, wherein the resulting red cells are not readily hemolyzed by any serum or plasma sample, for example by complement lysis. The RBC compns. are of particular use for introduction into an individual in cases where

the potential for an immune reaction is high, for example in alloimmunized blood recipients or in trauma situations where the possibility of transfusion of a mismatched unit of blood is higher. E.g., I was prepared from MeO(CH2CH2O)nCONH(CH2)5CO2H and NHS. One of the examples given is determination of agglutination reaction of RBC with I
and similar derivs. Hemolysis of modified RBC are also given.

IT **620597-19-5P**
(**preparation** of antigen masked red blood cells having reduced hemolysis by sera by modification with **PEG** derivs.)

RN 620597-19-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM C12Q

CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 15, 35

IT 122375-06-8P **620597-19-5P 620597-21-9P**
620597-23-1P
(**preparation** of antigen masked red blood cells having reduced hemolysis by sera by modification with **PEG** derivs.)

IT 693252-88-9P **705261-18-3P 705261-20-7P**
705261-21-8P
(**preparation** of antigen masked red blood cells having reduced hemolysis by sera by modification with **PEG** derivs.)

L24 ANSWER 7 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 141:59650 HCA

TITLE: Preparation of antigen masked red blood cells with reduced hemolysis by modification with PEG derivatives

INVENTOR(S): Stassinopoulos, Adonis; Clark, Basha

PATENT ASSIGNEE(S): Cerus Corporation, USA

SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050848	A2	20040617	WO 2003-US38224	20031203

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 2002-431213P	P	20021204
US 2002-431214P	P	20021204
US 2002-431215P	P	20021204
US 2002-431216P	P	20021204

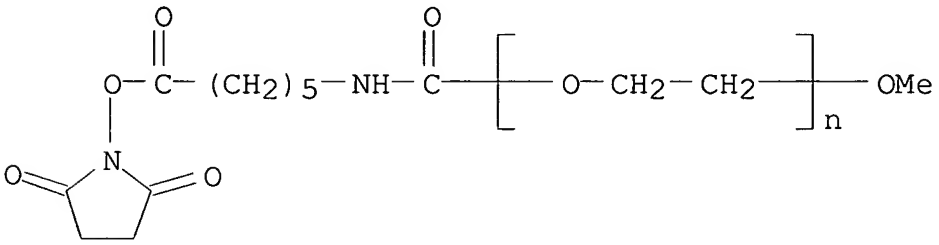
AB Methods are provided for the preparation of an RBC composition which has significantly reduced antigenicity. The methods of preparation of the red cell compns. involve the optimization of reaction conditions for attaching antigen masking compds. to the red cells without significantly affecting the function of the red cells, in particular reducing the hemolysis of the red cells from processing of the cells. The RBC compns. are of particular use for introduction into an individual in cases where the potential for an immune reaction is high, for example in allo-immunized blood recipients or in trauma

situations where the possibility of transfusion of a mismatched unit of blood in higher. The RBC compns. of this invention provide a much lower risk of a transfusion associated immune reaction. Thus, a derivative of PEG was prepared by from MeO(CH2CH2O)nCONH(CH2)5CO2H and NHS.

IT **620597-19-5P**
(**preparation** of antigen masked red blood cells with reduced hemolysis by modification with **PEG** derivs.)

RN 620597-19-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM C12N

CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 15, 35

IT 122375-06-8P **620597-19-5P 620597-21-9P**
620597-23-1P
(**preparation** of antigen masked red blood cells with reduced hemolysis by modification with **PEG** derivs.)

IT 9004-74-4DP, Methoxypolyethylene glycol, derivs. 693252-88-9P
705261-18-3P 705261-20-7P 705261-21-8P
(**preparation** of antigen masked red blood cells with reduced hemolysis by modification with **PEG** derivs.)

L24 ANSWER 8 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 141:59647 HCA

TITLE: Biological materials activated with polyethylene glycol compounds

INVENTOR(S): Stassinopoulos, Adonis; Zhou, Xue Min; Bowers, Simeon G.

PATENT ASSIGNEE(S): Cerus Corporation, USA

SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

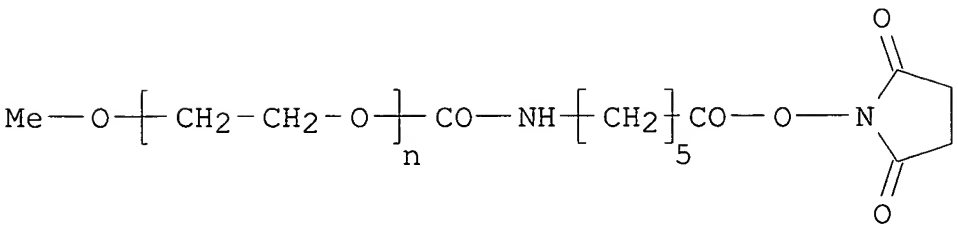
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050029	A2	20040617	WO 2003-US38262	20031203
WO 2004050029	A3	20041021		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:			US 2002-431213P	P 20021204
			US 2002-431214P	P 20021204
			US 2002-431215P	P 20021204
			US 2002-431216P	P 20021204

GI



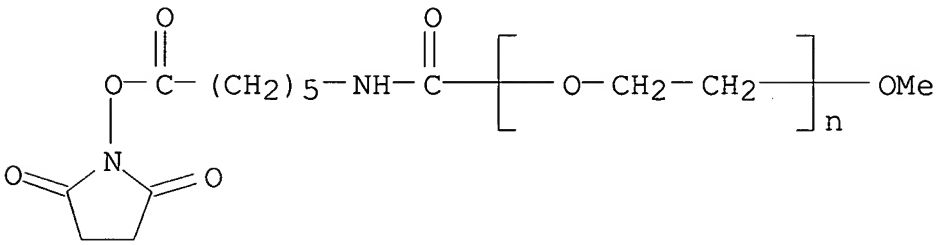
I

AB The present invention involves new polyethylene glycol derivs. that can be reacted with biol. materials to covalently attach the polyethylene glycol derivative to the material. The biol. materials may include proteins, liposomes, or cellular compns. The attachment of the polyethylene glycol to the materials results in improved biol. properties, such as reduced elimination of the materials by the immune system. In the case of red blood cells (RBC), the attachment of the compound provides either antigen masking of the red cells or improved viscosity of the red cells at low shear rates. E.g., I was prepared from MeO(CH2CH2O)nCONH(CH2)5CO2H and NHS. RBC were modified with I and a number of examples given showing improvement of properties of RBCs.

IT **620597-19-5P**
(biol. materials activated with **polyethylene glycol** compds.)

RN 620597-19-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM A61K

CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 35

IT 135649-01-3P 620597-18-4P **620597-19-5P** 620597-20-8P
620597-21-9P 620597-22-0P **620597-23-1P**
620597-24-2P 620597-25-3P 620597-26-4P 620597-27-5P
620597-28-6P 620597-29-7P 620597-30-0P 620597-31-1P
693252-88-9P **705261-18-3P** 705261-19-4P
705261-20-7P 705261-21-8P
(biol. materials activated with **polyethylene glycol** compds.)

L24 ANSWER 9 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:428862 HCA
TITLE: PEG-Ara-C conjugates for controlled release
AUTHOR(S): Schiavon, O.; Pasut, G.; Moro, S.; Orsolini, P.; Guiotto, A.; Veronese, F. M.

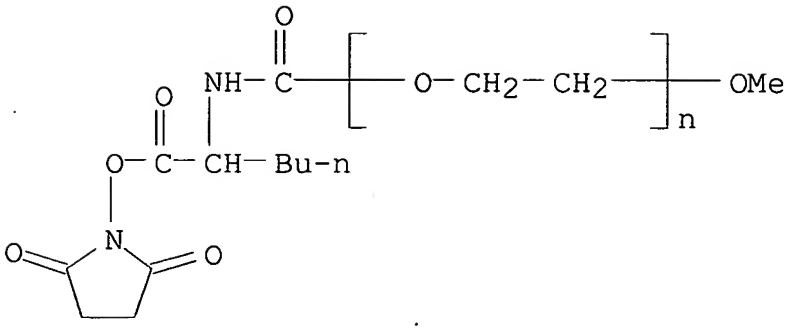
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Padua+, Padua, 35131, Italy
SOURCE: European Journal of Medicinal Chemistry (2004), 39(2), 123-133
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antitumor agent 1-β-D arabinofuranosylcytosine (Ara-C) was covalently linked to poly(ethylene glycol) (PEG) in order to improve the in vivo stability and blood residence time. Eight PEG conjugates were synthesized, with linear or branched PEG of 5000, 10000 and 20000 Da mol. weight through an amino acid spacer. Starting from mPEG-OH or HO-PEG-OH, conjugation was carried out to the one or two available hydroxyl groups at the polymer's extreme. Furthermore, to increase the drug loading of the polymer, the hydroxyl functions of PEG were functionalized with a bicarboxylic amino acid yielding a tetrafunctional derivative and, by recursive conjugation with the same bicarboxylic amino acid, products with four or eight Ara-C mols. for each PEG chain were prepared A computer graphic investigation demonstrated that aminoadipic acid was a suitable bicarboxylic amino acid to overcome the steric hindrance between the vicinal Ara-C mols. in the dendrimeric structure. In this paper we report the optimized conditions for synthesis and purification of PEG-Ara-C products with a low amount of remaining free drug, studies toward the hydrolysis of PEG-Ara-C and the Ara-C deamination by cytidine deaminase, pharmacokinetics in mice and cytotoxicity towards HeLa human cells were also investigated. Increased stability towards degradation of the conjugated Ara-C products, in particular for the highly loaded ones, improved blood residence time in mice and a reduced cytotoxicity with respect to the free Ara-C form was demonstrated.

IT **136372-28-6P**
(**PEG**-Ara-C conjugates for controlled release)

RN 136372-28-6 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[(1S)-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]pentyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 33
IT 124661-64-9P **136372-28-6P** 140218-03-7P 150673-50-0P
511274-90-1P 693243-65-1P **693243-66-2P**
693243-67-3P **693243-68-4P**
(**PEG**-Ara-C conjugates for controlled release)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 10 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:407546 HCA
TITLE: Novel hexa-arm polyethylene glycol and its derivatives and the methods of preparation thereof
INVENTOR(S): Kwang, Nho; Hyun, Chang-Min; Lee, Jung-Hun; Kim, In-Kyung; Pak, Young-Kyoung
PATENT ASSIGNEE(S): Sunbio Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004096507	A1	20040520	US 2002-326408	20021223
PRIORITY APPLN. INFO.:			KR 2002-69031	A 20021108

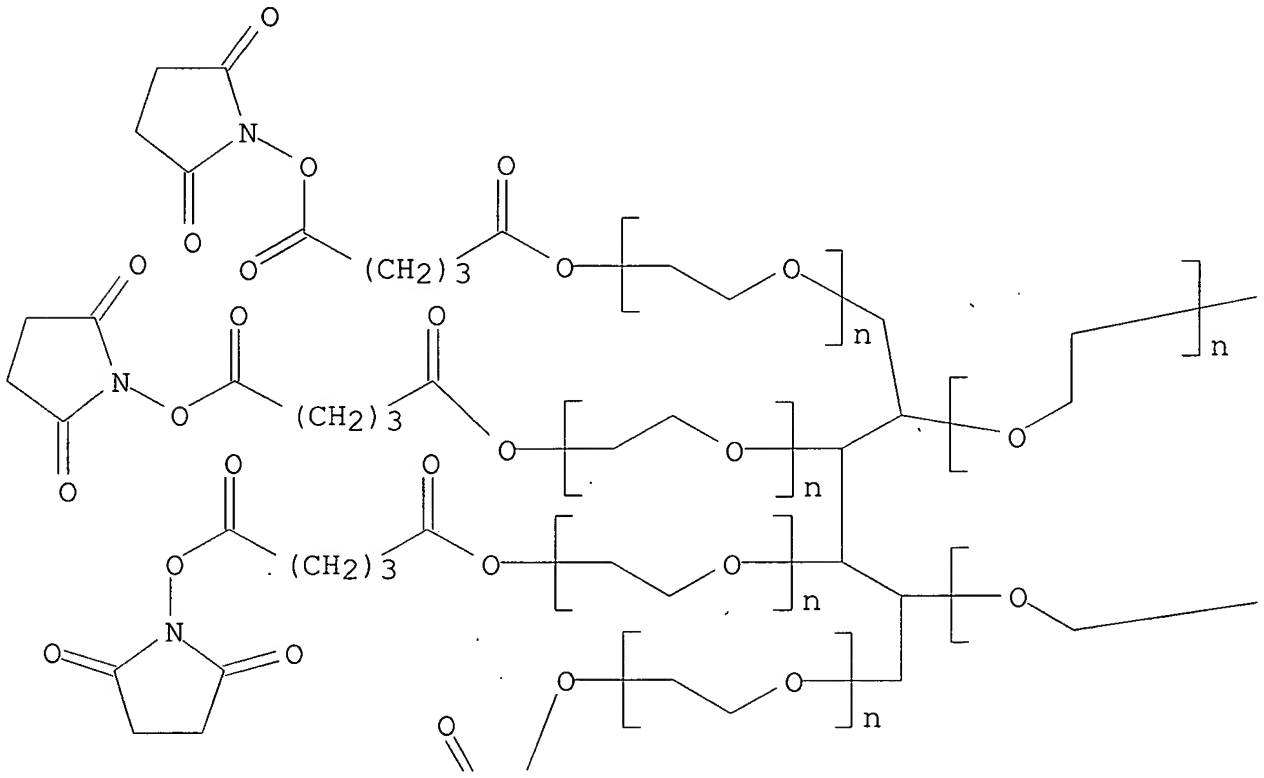
AB The core of 6-arm PEG derivs. is sorbitol and the end groups can be derivatized into many different reactive functionalities that are useful in conjugating with many different targets. The present invention also provides a biodegradable polymeric hydrogel-forming composition comprising the 6-arm PEG and its derivs., and methods of using such 6-arm PEG derivs. as surgical or biol. implants or sealants.

IT **690663-64-0P**
(manufacture of hexa-arm **polyethylene glycol** and its derivs. and their use)

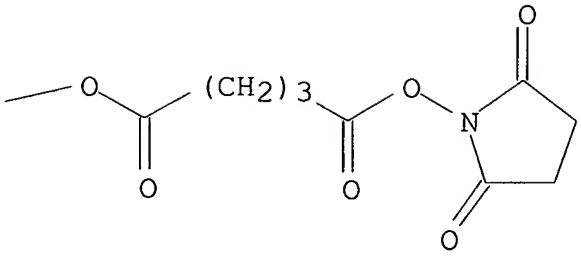
RN 690663-64-0 HCA

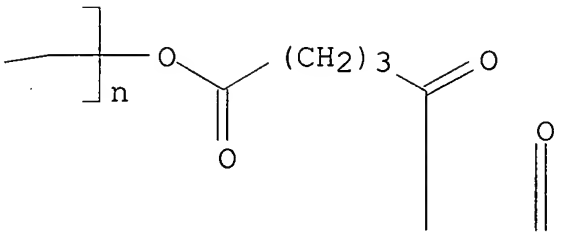
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-[[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]oxy]-, ether with D-glucitol (6:1) (9CI) (CA INDEX NAME)

PAGE 1-A

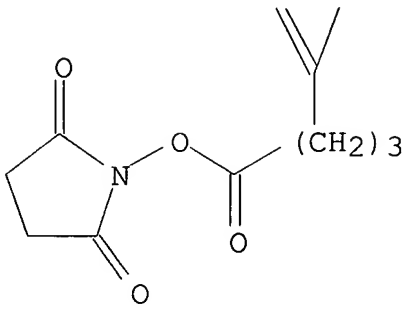


PAGE 1-B

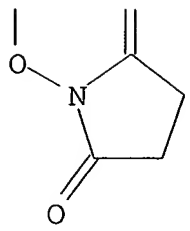




PAGE 2-A



PAGE 2-B



IC ICM C07C069-52
ICS A61K009-14; C08G059-00
NCL 424486000; 528405000; 560198000; 560200000
CC 37-3 (Plastics Manufacture and Processing)
Section cross-reference(s): 63
IT **690663-64-0P**
(manufacture of hexa-arm **polyethylene glycol** and its derivs. and their use)
IT 690663-65-1P **690663-67-3P** 690663-68-4P 690663-69-5P
690663-70-8P
(manufacture of hexa-arm **polyethylene glycol** and its derivs. and their use)

L24 ANSWER 11 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:380601 HCA
TITLE: Preparation of tree-type functionalized polyethylene glycol and its application as pharmaceutics
INVENTOR(S): Huang, Junlian; Huang, Zhaohua; Zhang, Haitao
PATENT ASSIGNEE(S): Fanya Biological Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 18 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1381512	A	20021127	CN 2002-101672	20020115
WO 2003059987	A1	20030724	WO 2003-CN29	20030101

15
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1479711 A1 20041124 EP 2003-701451
200301
15

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: CN 2002-101672 A
200201
15

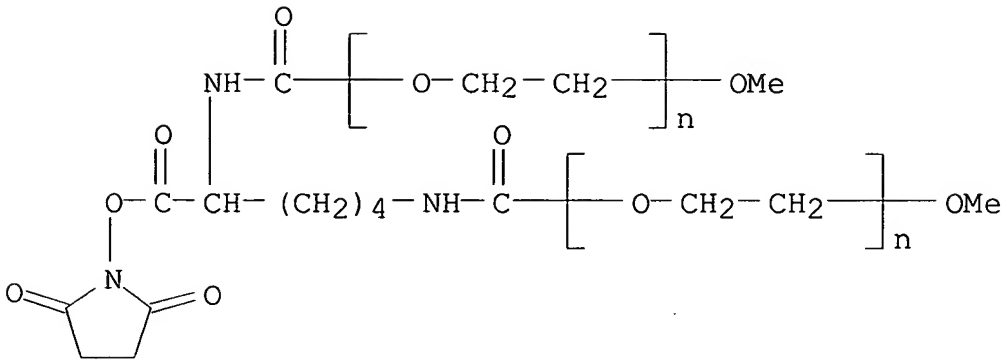
WO 2003-CN29 W
200301
15

AB The tree-type functional RPEGzCOX (R = C1-10 linear alkyl, iso-Pr or benzyl, preferably methyl; z = number of PEG branches, preferably 1-8; X = functional group such as H, OH, NH2, 2(3H)-methylene-5(4H)-oxo-1-pyrrolyloxy, 4-nitrophenoxy, 2-pyridyloxy or 2,5(3H,4H)-dioxo-1-pyrrolylmethoxy), is prepared by the stepwise reaction of polyethylene glycol (PEG) with a compound containing tri-functional groups such as H2N(CH2)nCH(NH2)COOH, 3,5-(or 3,4)-diaminophenyl-(CH2)m-COOH, 3,5-(or 3,4-)dihydroxyphenyl-(CH2)m-COOH or HO(CH2)n-CH(OH)COOH (n = 1-9; M = 0-6). The functionalized polyethylene glycol can be used as carrier for small mol. drugs (such as chlorambucil, cisplatin, 5-fluorouracil, taxol, adriamycin or methotrexate), peptide drugs or protein drugs (such as interferon, interleukin, tumor necrosis factor, growth factor, colony-stimulating factor, erythropoietin or superoxide dismutase).

IT **159540-80-4**
(**preparation** of tree-type functionalized **polyethylene glycol** and its application as pharmaceutics)

RN 159540-80-4 HCA

CN Poly(oxy-1,2-ethanediyl), α,α'-[[(1S)-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-1,5-pentanediyl]bis(iminocarbonyl)]bis[.omega.-methoxy- (9CI) (CA INDEX NAME)



IC ICM C08G065-48
ICS A61K031-74
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 35
IT 56-87-1, L-Lysine, reactions 657-27-2, L-Lysine hydrochloride
6066-82-6, N-Hydroxysuccinimide 124661-64-9 135649-01-3
159540-80-4 682806-76-4
(**preparation** of tree-type functionalized **polyethylene glycol** and its application as pharmaceutics)
IT 682806-73-1P **682806-77-5P** 682806-79-7P
682806-80-0P 682806-81-1P
(**preparation** of tree-type functionalized **polyethylene glycol** and its application as pharmaceutics)

L24 ANSWER 12 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:309204 HCA
TITLE: Biodegradable Poly(ethylene glycol)-co-poly(L-lysine)-g-histidine Multiblock Copolymers for Nonviral Gene Delivery
AUTHOR(S): Bikram, Malavosklish; Ahn, Cheol-Hee; Chae, Su Young; Lee, Minhyung; Yockman, James W.; Kim, Sung Wan
CORPORATE SOURCE: Department of Pharmaceutics, Pharmaceutical Chemistry Center for Controlled Chemical Delivery (CCCD), University of Utah, Salt Lake City, UT, 84112-5820, USA
SOURCE: Macromolecules (2004), 37(5), 1903-1916
CODEN: MAMOBX; ISSN: 0024-9297
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The development of biodegradable cationic polymers for use in

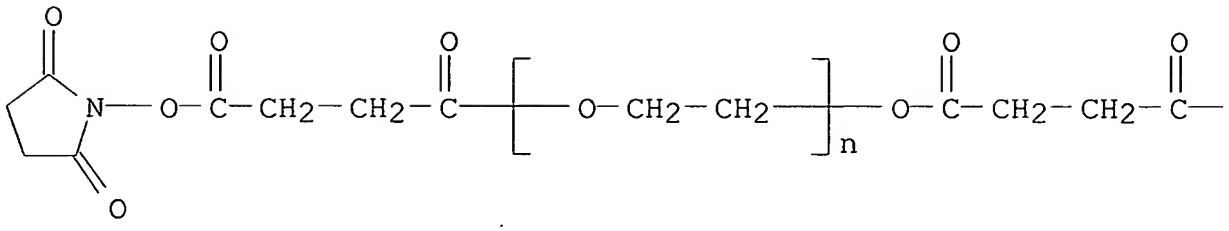
somatic gene therapy is desirable because degradable polymers have the potential to overcome cellular toxicities that are related to the high charge densities of the polycationic delivery system. Therefore, to produce a biocompatible gene delivery vehicle, we have designed a novel biodegradable, high mol. weight multiblock copolymer (MBC) of the type (AB)n which consists of repeating units of low mol. weight poly(ethylene glycol) (PEG) conjugated to low mol. weight cationic poly(L-lysine) (PLL). PEG was used not only to impart steric stabilization properties onto the polymer/pDNA complexes but also to introduce biodegradable ester bond linkages into the backbone of the MBCs. Also, to improve the endosome-disrupting capabilities of the polymer, N,N-dimethylhistidine (His) was coupled at various mole ratios (5 mol % His, 9 mol % His, 16 mol % His, 22 mol % His) to the ε-amines of PLL to produce PEG-PLL-grafted-His (PEG-PLL-g-His) MBCs. Polymer screening revealed that MBCs with 16% His grafted (PEG-PLL-g-16% His) (31 kDa) produced the highest transfection efficiency with minimal cytotoxicity in murine smooth muscle cells (A7r5). The MBCs condensed plasmid DNA (pDNA) into nanostructures with an average particle size between 150 and 200 nm with no aggregation and surface charge of .apprx.4-45 mV. These MBCs also protected pDNA from endonuclease digestion for at least 2 h. The polymers showed exponential decay with a half-life (t1/2) of .apprx.5 h in PBS, pH 7.4 at 37 °C. However, complexes incubated in PBS buffer showed complete stability up to 6 days despite the short polymer t1/2. The pK of the conjugated imidazoles was found to be 4.75 which would facilitate buffering at low pH environments of the late endosome/lysosome. Finally, the ability of the imidazoles to protonate and destabilize membrane vesicles was investigated by the use of bafilomycin A1 which showed that the MBCs produced about five times higher transfection efficiency in vitro in A7r5 cells compared to the treated cells. This supports the function of histidine as an endosomal disrupting moiety. Therefore, these results suggest that biodegradable multiblock copolymers are promising candidates for long-term gene delivery.

IT **85419-94-9P**
(biodegradable **polyethylene glycol** -co-poly(L-lysine)-g-histidine multiblock copolymers for nonviral gene delivery)

RN 85419-94-9 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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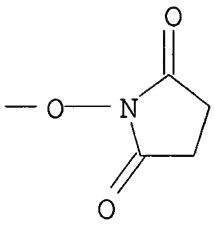


CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 34, 35

IT 1676-86-4P 24940-57-6DP, N,N-Dimethyl-L-histidine, reaction products with block ethoxylated polylysine derivs. 37684-51-8P, Polyethylene glycol disuccinate **85419-94-9P** **677030-45-4P**
(biodegradable **polyethylene glycol** -co-poly(L-lysine)-g-histidine multiblock copolymers for nonviral gene delivery)

IT **677030-45-4DP**, deprotected, histidine-conjugated
(biodegradable **polyethylene glycol** -co-poly(L-lysine)-g-histidine multiblock copolymers for nonviral gene delivery)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 13 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:169625 HCA
TITLE: **Polyalkylene glycol** acid conjugates
INVENTOR(S): Bailon, Pascal Sebastian; Won, Chee-Youb
PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

Applicants

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004012773	A1	20040212	WO 2003-EP7736	20030716
US 2004106747	A1	20040603	US 2003-625033	20030722

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

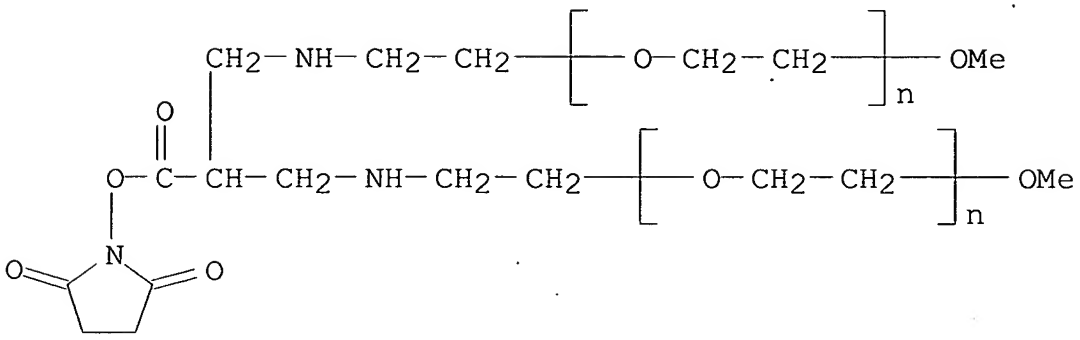
PRIORITY APPLN. INFO.: US 2002-398137P P 20020724

AB A new class of activated **polyalkylene glycol** acids and their active ester reagents for conjugation to biopharmaceuticals such as polypeptides, sugars, proteins and therapeutically active small mols. to produce biol. active conjugates of these pharmaceuticals and methods for producing these conjugates are disclosed. Alpha-methoxy, omega-valeric acid succinimidyl ester of PEG (preparation given) was conjugated to T-20 (a polypeptide).

IT **656820-43-8P**
(**polyalkylene glycol** acid conjugates)

RN 656820-43-8 HCA

CN Poly(oxy-1,2-ethanediyl), α,α'-[[2-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-1,3-propanediyl]bis(imino-2,1-ethanediyl)]bis[ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM A61K047-48
ICS C08G065-332; C08G065-337; C08G065-329
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 35
ST **polyalkylene glycol** acid peptide protein conjugate
IT Peptides, biological studies
Proteins
(conjugates, **polyalkylene glycol** acids; **polyalkylene glycol** acid conjugates)
IT 6066-82-6 7425-49-2 9004-74-4 14660-52-7, Ethyl-5-bromovalerate
(**polyalkylene glycol** acid conjugates)
IT 656820-37-0P 656820-38-1P 656820-41-6P **656820-43-8P**
(**polyalkylene glycol** acid conjugates)
IT 30516-87-1, Azt 159519-65-0, t-20
(**polyalkylene glycol** acid conjugates)
IT **656820-39-2P 656820-40-5P**
(**polyalkylene glycol** acid conjugates)
IT 656820-42-7P
(**polyalkylene glycol** acid conjugates)

L24 ANSWER 14 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:151785 HCA
TITLE: Multi-component DNA delivery system AsOR-PL/PEG-PEI targeted for liver
AUTHOR(S): Jin, Xueyuan; Zhang, Lingxia; Lou, Min; Xie, Jianfang
CORPORATE SOURCE: The 5th Division, 302th Hospital of PLA, Beijing, 100039, Peop. Rep. China
SOURCE: Shijie Huaren Xiaohua Zazhi (2002), 10(3), 295-298
CODEN: SHXZF2; ISSN: 1009-3079
PUBLISHER: Shijie Weichangbingxue Zazhishe
DOCUMENT TYPE: Journal

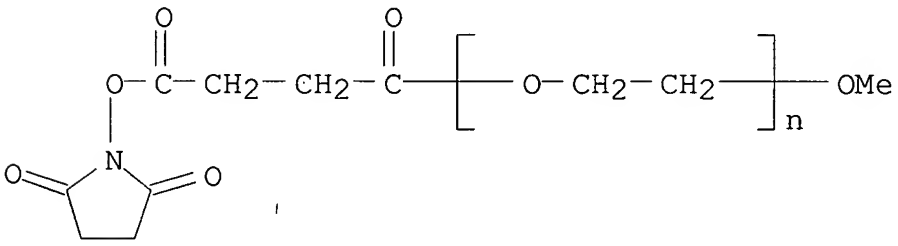
LANGUAGE: Chinese

AB A multi-component DNA delivery system which incorporated hepatocyte targeting ligand, DNA compressing domain and endosome disruptive mol. in one complex, were developed. Asialoorosomucoid (AsOR) was conjugated to polylysine (PL) by EDC. The active ester of polyethylene glycol (PEG) derivative was reacted with the amino groups in polyethylenimine (PEI) to form PEG-PEI conjugate. DNA was first complexed with PEG-PEI and then with AsOR-PL. In vitro the transfection experiment was conducted in the galactose receptor pos. Huh-7 cells. In vivo the transduction was also evaluated in mice after tail vein injection. AsOR-PL/ PEG-PEI/DNA was able to effectively deliver luciferase gene into the galactose receptor pos. Huh-7 cells in vitro. The transfection was specifically inhibited by the synthesized ligand-lactosaminated bovine serum albumin (BSA). After tail vein injection, the reporter gene was expressed specifically in the liver of mice. The multi-component system of AsOR-PL and PEG-PEI can be used as a specific and efficient DNA carrier.

IT **78274-32-5DP**, Methoxy **polyethylene glycol** N-succinimidyl succinate, reaction product with polyethylenimine (multi-component DNA delivery system AsOR-PL/**PEG**-PEI targeted for liver)

RN 78274-32-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 63-6 (Pharmaceuticals)

IT 9002-98-6DP, Polyethylenimine, reaction product with PEG derivative
25104-18-1DP, Polylysine, conjugate with asialoorosomucoid
38000-06-5DP, Polylysine, conjugate with asialoorosomucoid
78274-32-5DP, Methoxy **polyethylene glycol** N-succinimidyl succinate, reaction product with polyethylenimine (multi-component DNA delivery system AsOR-PL/**PEG**-PEI targeted for liver)

L24 ANSWER 15 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 140:65210 HCA

TITLE: Preparation of PEG-treated factor VII glycoforms

INVENTOR(S): Klausen, Niels Kristian; Bjorn, Soren; Behrens,

Carsten; Garibay, Patrick William
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000366	A1	20031231	WO 2003-DK420	20030620

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DK 2002-964 A 20020621
US 2002-394778P P 20020701

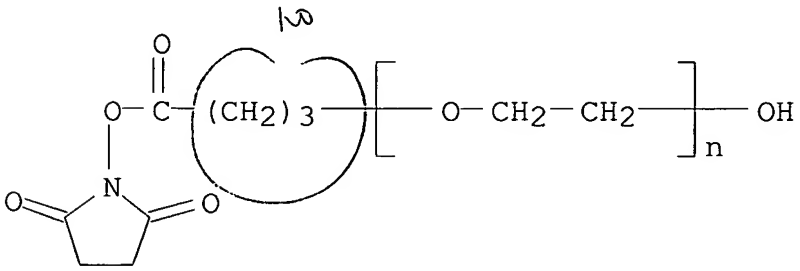
AB The invention concerns a formulation comprising a plurality of Factor VII polypeptides or Factor VII-related polypeptides, wherein the polypeptides comprise asparagine-linked and/or serine-linked oligosaccharide chains, and wherein at least 1 oligosaccharide group is covalently attached to at least one polymeric group. The polymeric group could be a polyalkylene oxide (PAO), e.g., polyethylene glycol (PEG). PEG-CMP-sialic acid (PEG-CMPSA) is prepared by covalently attaching PEG with mol. weight 10,000 Da to sialic acid by treating Factor VIIa with 87-93% content of sialic acid with sialyltransferase by using PEGCMPSA as donor mol. After the PEGylation reaction has reached maximal incorporation, CMPSA is added to the reaction mixture to cap any exposed terminal galactose.

Incorporation of PEGylated sialic acid is analyzed by SDS-PAGE, CE-PAGE, isoelec. focusing gels, and CE-IEF.

IT **196936-07-9**
(**preparation** of **PEG**-treated factor VII glycoforms)

RN 196936-07-9 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IC ICM A61K047-48
ICS A61K038-36; C12N009-64; C07K014-745; A61P007-02; A61P007-04

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 13

IT **196936-07-9** 638199-44-7
(**preparation** of **PEG**-treated factor VII glycoforms)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 16 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 139:385993 HCA

TITLE: Preparation and characterization of folate-targeted pEG-coated pDMAEMA-based polyplexes

AUTHOR(S): van Steenis, J. H.; van Maarseveen, E. M.; Verbaan, F. J.; Verrijk, R.; Crommelin, D. J. A.; Storm, G.; Hennink, W. E.

CORPORATE SOURCE: Utrecht Institute for Pharmaceutical Sciences (UIPS), Department of Pharmaceutics, Utrecht University, Utrecht, 3508 TB, Neth.

SOURCE: Journal of Controlled Release (2003), 87(1-3), 167-176
CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A folate-poly(ethylene glycol) conjugate capable of covalent coupling to primary amines present at the surface of polyplexes was developed. Coating of poly(dimethylaminomethyl methacrylate) (pDMAEMA)-based polyplexes with this folate-pEG conjugate led to a

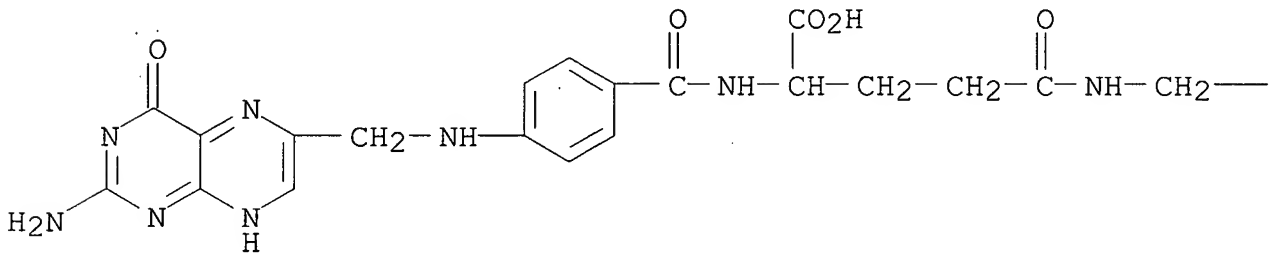
sharp decrease of the ζ-potential, and a small increase in particle size. The size of the particles in isotonic medium did not change markedly in time demonstrating that rather stable particles were formed. The in vitro cellular toxicity of the pEGylated polyplexes with and without folate ligands was lowered considerably compared to uncoated polyplexes. The toxicity observed for the targeted pEGylated polyplexes was slightly higher than that of corresponding untargeted polyplexes, which might indicate an increased cellular association of targeted polyplexes. Transfection of OVCAR-3 cells in vitro was markedly increased compared to untargeted pEGylated polyplexes, suggesting targeted gene delivery.

IT **623947-12-6P**
(folate-targeted **PEG**-coated pDMAEMA-based DNA polyplexes)

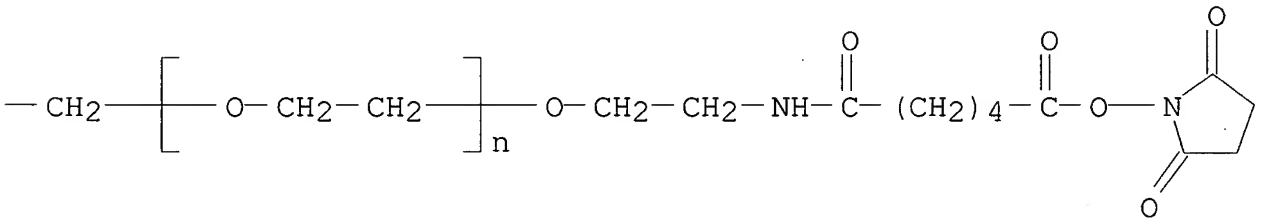
RN 623947-12-6 HCA

CN Poly(oxy-1,2-ethanediyl), α-[2-[[(4S)-4-[[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]amino]-4-carboxy-1-oxobutyl]amino]ethyl]-ω-[2-[[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,6-dioxohexyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



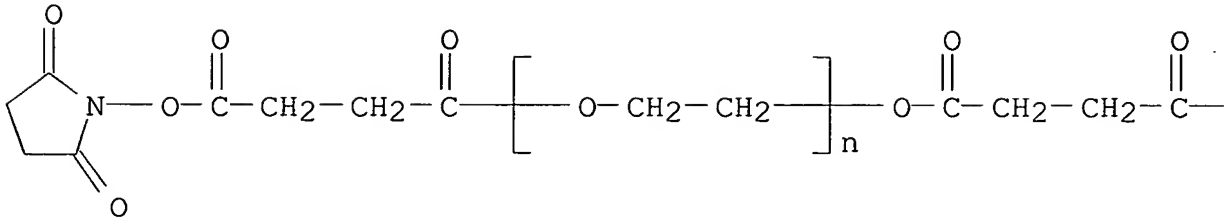
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3

IT 482648-85-1P **623947-12-6P**

(folate-targeted **PEG**-coated pDMAEMA-based DNA polyplexes)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 17 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:354251 HCA
TITLE: Preparation and antitumor effect of drug delivery system of taxol conjugated to polyethylene glycol
AUTHOR(S): Feng, Xia; Liang, Shile; Li, Xiaofeng; Yuan, Yingjin
CORPORATE SOURCE: Department of Pharmaceutical Engineering, School of Chemical Engineering and Technology, Tianjin University, Tianjin, 300072, Peop. Rep. China
SOURCE: Huagong Xuebao (Chinese Edition) (2003), 54(2), 209-214
CODEN: HUKHAI; ISSN: 0438-1157
PUBLISHER: Huaxue Gongye Chubanshe, Huagong Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A novel drug delivery system (DDS) of taxol was developed by linking taxol to a water-soluble polymer-polyethylene glycol (PEG) through amino acid spacer. Solubility of the DDS and content of taxol in them were determined Their antitumor activity were evaluated against two human tumor cell lines: MCF-7 and PG. It was found that the DDS were more soluble in water than taxol and had similar cytotoxicity compared with the latter. In this way, a new kind of DDS of taxol with improved water-solubility and potential antitumor activity was well established.
IT **85419-94-9P**
(**preparation** and antitumor effect of drug delivery system of taxol conjugated to **polyethylene glycol**)
RN 85419-94-9 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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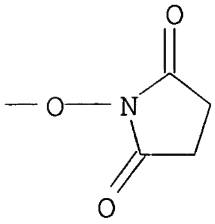


CC 63-5 (Pharmaceuticals)
IT 37684-51-8P **85419-94-9P** 468066-16-2P 468066-17-3P
468066-18-4P 468066-19-5P 468066-20-8P 543726-11-0P
543726-13-2P 543726-14-3P
(**preparation** and antitumor effect of drug delivery system of taxol conjugated to **polyethylene glycol**)

L24 ANSWER 18 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:308097 HCA
TITLE: Synthesis and characterization of thiol-terminated poly(ethylene oxide) for chemisorption to gold surface
AUTHOR(S): Du, Ying Jun; Brash, John L.
CORPORATE SOURCE: Department of Chemical Engineering, McMaster University, Hamilton, ON, L8S 4L7, Can.
SOURCE: Journal of Applied Polymer Science (2003), 90(2), 594-607
CODEN: JAPNAB; ISSN: 0021-8995
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thiol-terminated poly(ethylene oxide) (PEO) was synthesized using two different approaches: esterification of terminal hydroxyl groups with mercaptoacetic acid and amidation using N-**hydroxysuccinimidyl** PEO (NHS-PEO) and cysteine. The reaction of hydroxyl-terminated PEO with mercaptoacetic acid was

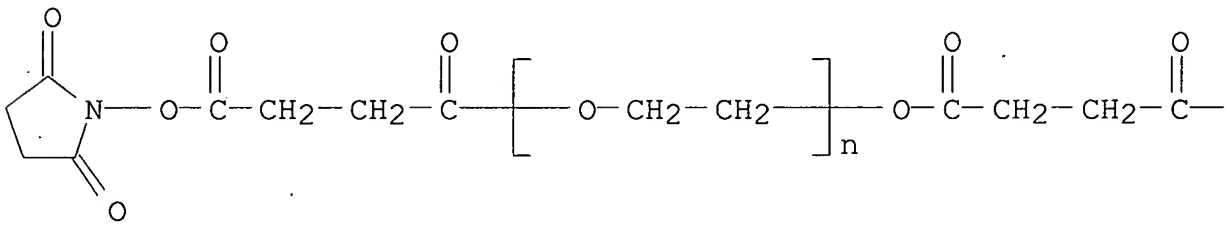
carried out in boiling toluene. Different thiolated PEOs, including linear PEOs of varying mol. wts. and end-group types, and star-type PEOs were synthesized. NMR and IR spectroscopy were used to characterize the products. The reaction kinetics were also briefly investigated. Gel permeation chromatog. was used to investigate the relative amts. of the mono- and disubstituted products in the α,ω-dihydroxy PEOs. NHS-PEO was used both to attach terminal thiol groups via reaction with cysteine and to conjugate other amino acids (and potentially any amino-containing mol.) to PEO. Reactions using NHS-PEO were carried out at room temperature in water. The chemisorption of these thiolated PEOs to gold was expected to yield surfaces resistant to biofouling, in particular to unwanted protein adsorption. Chemisorption of amino acid-, peptide-, or protein-terminated PEOs in addition may yield surfaces having specific biol. activity. Work on these aspects will be reported elsewhere.

IT **85419-94-9**
(synthesis and characterization of thiol-terminated poly(ethylene oxide) for chemisorption to gold surface)

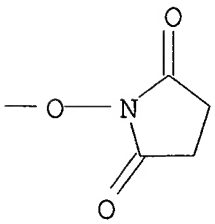
RN 85419-94-9 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



CC 35-8 (Chemistry of Synthetic High Polymers)
Section cross-reference(s): 56

IT 52-90-4, Cysteine, reactions 56-87-1, Lysine, reactions

108-30-5, Succinic anhydride, reactions 616-34-2, Glycine methyl ester 6066-82-6, N-Hydroxysuccinimide **85419-94-9**
(synthesis and characterization of thiol-terminated poly(ethylene oxide) for chemisorption to gold surface)

IT 68-11-1DP, Mercaptoacetic acid, reaction products with 8-arm **polyethylene glycol** 25322-68-3DP, **Polyethylene glycol**, 8-arm derivs., reaction products with mercaptoacetic acid 37684-51-8P 63143-05-5P 63666-80-8P 68865-56-5P **78274-32-5P** 165747-32-0P 612095-93-9P 612095-94-0P 612095-95-1P 612095-96-2P
(synthesis and characterization of thiol-terminated poly(ethylene oxide) for chemisorption to gold surface)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 19 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 139:242588 HCA

TITLE: Immobilization of cells and liposomes via amphipathic coupling reagent, activated ester of polyethylene glycol oleyl ether

INVENTOR(S): Nagamune, Teruyuki; Miyake, Jun; Miyake, Masato; Kato, Koichi

PATENT ASSIGNEE(S): National Institute of Advanced Industrial Science and Technology, Japan

SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074691	A1	20030912	WO 2003-JP2340	20030228

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG
EP 1489167 A1 20041222 EP 2003-743527 200302 28
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: JP 2002-55459 A 200203 01
WO 2003-JP2340 W 200302 28

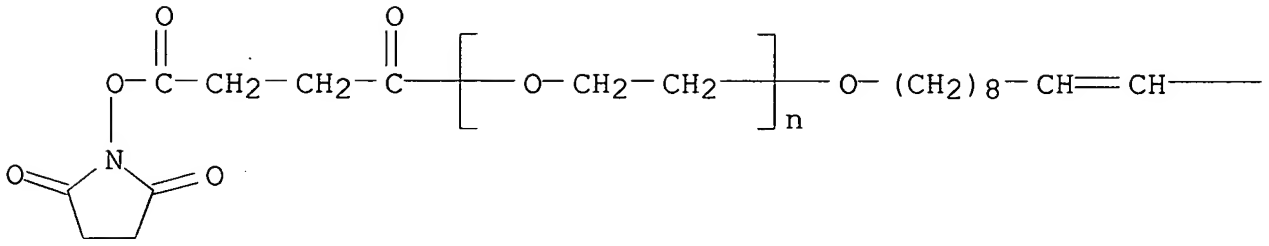
AB A method of immobilizing suspended cells, phospholipid vesicles or the like on a solid phase surface regardless of the cell type, is disclosed. The cells are brought into contact with a support having a hydrophobic chain and a hydrophilic chain and immobilized thereon. Immobilizing agent comprises hydrophobic chains composed of optionally substituted saturated or unsatd. hydrocarbon chains, lipids or lipid complex constituting a cell membrane. The hydrophilic chain comprises protein, oligonucleotide, polymer or copolymer of glycolic acid, lactic acid, and p-dioxane, oligopeptide, polypeptide, polyamide, polyamide, **polyalkylene glycol**, or polysaccharide. The hydrophilic chain may be polyethylene glycol, containing functional **group** such as **activated** ester, such as polyethylene-oxide-oleyl ether-N-hydroxy succinimide ester. The immobilizing agent comprises protein, peptide, silane coupling reagent, functional group-containing polymer. The support may have a gene introduced in it. Culturing method for immobilized cells is also claimed. Immobilization of various cell types using poly(ethylene glycol) oleyl ether (PEG-Ole) is described. Liposomes (cationic, weakly neg. charged, and anionic) were also immobilized.

IT **496050-85-2**
(immobilization of cells using; immobilization of cells and liposomes via amphipathic coupling reagent, activated ester of polyethylene glycol oleyl ether)

RN 496050-85-2 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-[(9Z)-9-octadecenyloxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

— $(CH_2)_7$ — Me

IC ICM C12N011-06
ICS C12N001-00
CC 9-16 (Biochemical Methods)
IT **496050-85-2**
(immobilization of cells using; immobilization of cells and liposomes via amphipathic coupling reagent, activated ester of polyethylene glycol oleyl ether)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

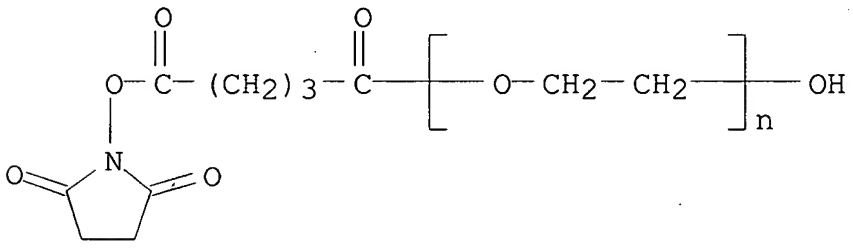
L24 ANSWER 20 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:117782 HCA
TITLE: Synthesis of Polyethylene Glycol (PEG) Derivatives and PEGylated-Peptide Biopolymer Conjugates
AUTHOR(S): Li, Jing; Kao, W. John
CORPORATE SOURCE: Division of Pharmaceutical Sciences of the School of Pharmacy and Department of Biomedical Engineering of the College of Engineering, University of Wisconsin, Madison, WI, 53705, USA
SOURCE: Biomacromolecules (2003), 4(4), 1055-1067
CODEN: BOMAF6; ISSN: 1525-7797
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We synthesized a library of 50 poly(ethylene glycol) (PEG) derivs. to expand the extent of conjugation with biol. active mols.

(biopolymers, peptides, drugs, etc.) and biomaterial substrates. The formation of PEG derivs. was confirmed with HPLC, 1H and 13C NMR. PEG derivs. were polymerized into networks in order to study the role of PEG and terminal functional groups in modulating the hydrophilicity of biomaterials and cell-biomaterial interaction. The resulting surface hydrophilicity and the number of adhered fibroblasts were primarily dependent on the PEG concentration with the mol.
weight and the terminal functional group of PEG derivs. being less important. One of PEG derivs., PEG-bis-glutarate, was utilized to link peptide sequences to gelatin backbone in the formation of novel biomedical hydrogels. PEG-peptide conjugates were characterized by mass spectroscopy. PEG-peptide modified gelatins were characterized by gel permeation chromatog.

IT **108188-71-2P**
(synthesis of **polyethylene glycol** derivs. and polyethoxylated peptide biopolymer conjugates)

RN 108188-71-2 HCA

CN Poly(oxy-1,2-ethanediyl), α-[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



CC 35-8 (Chemistry of Synthetic High Polymers)
Section cross-reference(s): 34, 63

IT 26403-58-7P, Polyethylene glycol monoacrylate 26570-48-9P, Polyethylene glycol diacrylate 32171-39-4P, Polyethylene glycol acrylate monomethyl ether 35164-96-6P 39828-93-8P 39927-06-5P 39927-08-7P 41705-20-8P 58320-73-3P 67665-18-3P 67665-19-4P 73342-22-0P 73464-20-7P 75716-40-4P 76378-39-7P 79934-70-6P 95934-91-1P **108188-71-2P 111575-54-3P** 117521-16-1P 118738-47-9P 151039-90-6P **154467-38-6P** 157598-59-9P 172884-76-3P 416846-07-6P 416846-08-7P 416846-09-8P 562871-03-8P 562871-04-9P 562871-05-0P 562871-06-1P 562871-07-2P 562871-08-3P 562871-09-4P 562871-10-7P 562871-11-8P 562871-12-9P 562871-13-0P 562871-14-1P 562871-15-2P 562871-16-3P 562871-17-4P 562871-18-5P 562871-19-6P 562871-20-9P 562871-21-0P **562871-22-1P 562871-23-2P 562871-24-3P**
(synthesis of **polyethylene glycol** derivs. and polyethoxylated peptide biopolymer conjugates)

REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

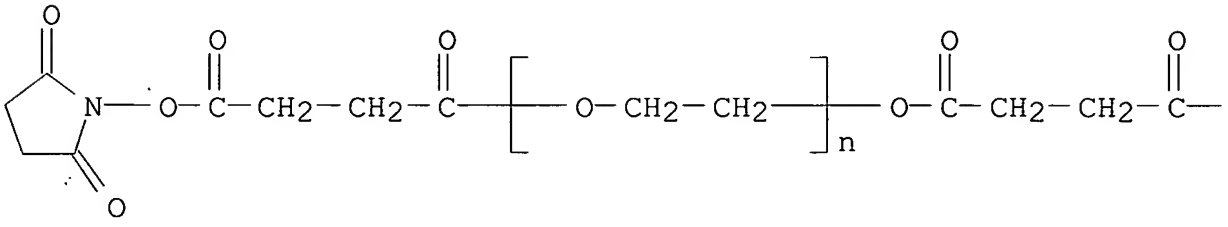
L24 ANSWER 21 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:90322 HCA
TITLE: The use of bifunctional **polyethylene glycol** derivatives for coupling of proteins to and crosslinking of collagen matrices
AUTHOR(S): Chen, J.-S.; Noah, E. M.; Pallua, N.; Steffens, G. C. M.
CORPORATE SOURCE: Institute of Biochemistry, Aachen University of Technology, Aachen, Germany
SOURCE: Journal of Materials Science: Materials in Medicine (2002), 13(11), 1029-1035
CODEN: JSMMEL; ISSN: 0957-4530
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The realization of three-dimensional (3D) degradable matrixes which slowly release bio-active components represents a major challenge in the field of tissue engineering. In this paper we report on the usage of com. available bifunctional agents for both the covalent coupling of proteins to and the crosslinking of collagen matrixes. Proteins - horse radish peroxidase (HRP) was used as a model protein - were cross-linked with either a homobifunctional (disuccinimidyl disuccinate **polyethylene glycol**) or a heterobifunctional (N-**hydroxy succinimidyl** vinyl sulfone polyethyleneglycol) agent. In the case of the heterobifunctional crosslinking agent the collagen matrixes were previously modified with succinimidyl acetyl thioacetate in order to introduce sulfhydryl groups. As compared with control expts. a 10-fold and 50-fold increase of immobilized proteins were achieved with the homobifunctional and heterobifunctional cross-linker resp. The HRP-**PEG** conjugates demonstrated a better long-term stability as compared to the non-treated HRP. The effects of the crosslinking agents and the thiolation reagent succinimidylacetylthio acetate on the in vitro degradation of the collagen matrixes by collagenase were also investigated. In particular the reaction with succinimidylacetylthio acetate appears to offer interesting opportunities both for coupling active proteins and modulating the degradation times of collagen matrixes.

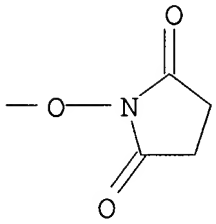
IT **85419-94-9DP**, conjugates with peroxidase (bifunctional **polyethylene glycol** derivs. used for coupling of proteins to and crosslinking of collagen matrixes)
RN 85419-94-9 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



CC 63-7 (Pharmaceuticals)

ST **polyethylene glycol** deriv peroxidase collagen crosslinking bioadhesion degrdn

IT Adhesion, biological
Stability
(bifunctional **polyethylene glycol** derivs. used for coupling of proteins to and crosslinking of collagen matrixes)

IT Decomposition
(biodegrdn.; bifunctional **polyethylene glycol** derivs. used for coupling of proteins to and crosslinking of collagen matrixes)

IT Animal tissue
(engineering; bifunctional **polyethylene glycol** derivs. used for coupling of proteins to and crosslinking of collagen matrixes)

IT Collagens, biological studies
(type I, conjugates with succinimidyl acetyl thioacetate; bifunctional **polyethylene glycol** derivs. used for coupling of proteins to and crosslinking of collagen matrixes)

IT **85419-94-9DP**, conjugates with peroxidase

(bifunctional **polyethylene glycol** derivs.
used for coupling of proteins to and crosslinking of collagen matrixes)
IT 417707-58-5D, conjugate with peroxidase
(bifunctional **polyethylene glycol** derivs.
used for coupling of proteins to and crosslinking of collagen matrixes)
IT 76931-93-6DP, Succinimidyl acetyl thioacetate, conjugate with collagen
(bifunctional **polyethylene glycol** derivs.
used for coupling of proteins to and crosslinking of collagen matrixes)
IT 9003-99-0D, Peroxidase, conjugate with **polyethylene glycol** derivs.
(horse radish; bifunctional **polyethylene glycol** derivs. used for coupling of proteins to and crosslinking of collagen matrixes)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 22 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 139:26651 HCA
TITLE: Modified lipids as delivery vehicles for therapeutic agents
INVENTOR(S): Jorgensen, Michael; Keller, Michael; Miller, Andrew David; Perouzel, Eric
PATENT ASSIGNEE(S): Mitsubishi Chemical Corporation, Japan
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047549	A2	20030612	WO 2002-GB5471	20021204
WO 2003047549	A3	20031231		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1455834 A2 20040915 EP 2002-783264 200212 04

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.: GB 2001-29121 A 200112 05

WO 2002-GB5471 W 200212 04

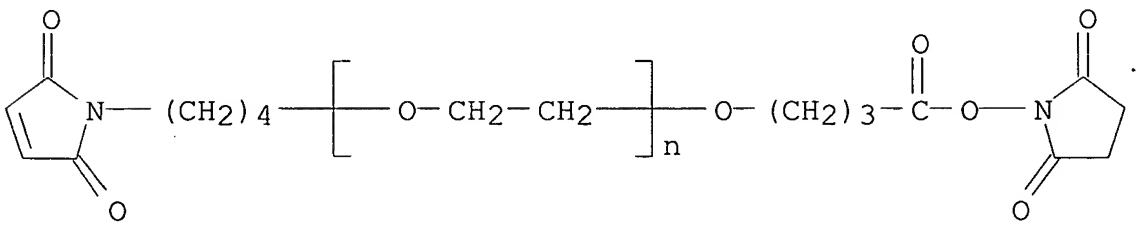
OTHER SOURCE(S): MARPAT 139:26651

AB The present invention provides a delivery vehicle for a therapeutic agent comprising a modified lipid and a therapeutic agent (e.g., DNA); wherein the modified lipid comprises a lipid and a delivery, targeting or stabilizing moiety (DTS moiety); wherein the lipid is linked to the DTS moiety via a linker which is stable in biol. fluid and which is unstable in defined conditions; and wherein the DTS moiety is linked to the lipid alter formation of a complex of lipid and therapeutic agent. Thus, a cholesterol-containing lipid was obtained by the reaction of a cholesterol derivative with a serine derivative Liposomes were obtained from DOPE and the above lipid. The addition of PEG dialdehyde stabilized the liposomes.

IT **539792-10-4**
(in **preparation** of **PEG**-lipid systems; modified lipids as delivery vehicles for therapeutic agents)

RN 539792-10-4 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)butyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]- (9CI) (CA INDEX NAME)



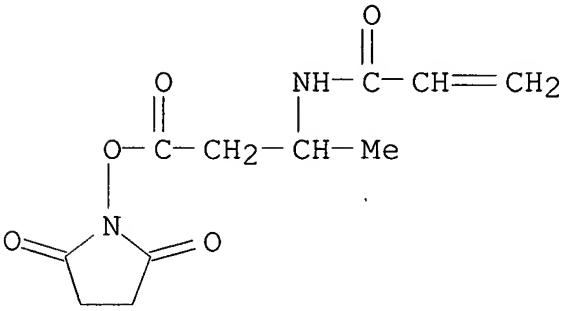
IC ICM A61K009-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 32, 34
IT 56-40-6, Glycine, reactions 107-15-3, 1,2-Ethanediamine, reactions 141-43-5, reactions 156-87-6, 3-Aminopropanol 302-01-2, Hydrazine, reactions 771-61-9, Pentafluorophenol 870-46-2 6318-55-4 7144-08-3 13734-38-8 21947-98-8 22483-09-6 34901-14-9 56976-06-8 **539792-10-4**
(in **preparation** of **PEG**-lipid systems; modified lipids as delivery vehicles for therapeutic agents)

L24 ANSWER 23 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:386127 HCA
TITLE: Newly designed hydrogel with both sensitive thermoresponse and biodegradability
AUTHOR(S): Yoshida, Takatsune; Aoyagi, Takao; Kokufuta, Etsuo; Okano, Teruo
CORPORATE SOURCE: Institute of Applied Biochemistry, University of Tsukuba, Ibaraki-ken, 305-8572, Japan
SOURCE: Journal of Polymer Science, Part A: Polymer Chemistry (2003), 41(6), 779-787
CODEN: JPACEC; ISSN: 0887-624X
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis and characterization of thermoresponsive hydrogels on the basis of N-isopropylacrylamide (IPAAm) copolymers crosslinked with biodegradable poly(amino acids) are described. This hydrogel was prepared with two kinds of reactive IPAAm-based copolymers containing poly(amino acids) as the side-chain **groups** and **activated** ester **groups**. We introduced the graft chains by decarboxylation polymerization of amino acid N-carboxyanhydrides initiated from lateral amino groups in the PIPAAm copolymer. The hydrogels easily crosslinked with degradable poly(amino acid) chains by only mixing the copolymer aqueous solns. The gelling method in this study would provide some of the following innovative features:. (1) No necessary removal of unreacted monomers and so forth,. (2) Simpler loading of drugs into the hydrogels (only mixing when gelling), and. (3) Easier insertion into the body. On the basis of the swelling ratio measurement of the hydrogel, large volume changes dependent on temperature changes were observed Moreover, the enzymic temperature-dependent degradation was confirmed. The results suggested that these hydrogels could be used for an injectable or implantable matrix of temperature-modulated drug release.

IT **528583-46-2P**
(hydrogel with both sensitive thermoresponse and biodegradability)
RN 528583-46-2 HCA
CN 2-Propenamide, N-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1-methyl-3-oxopropyl]-, polymer with N-(1-methylethyl)-2-propenamide (9CI) (CA INDEX NAME)

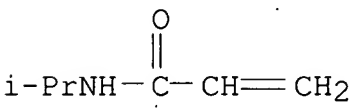
CM 1

CRN 528583-45-1
CMF C11 H14 N2 O5



CM 2

CRN 2210-25-5
CMF C6 H11 N O



CC 37-3 (Plastics Manufacture and Processing)
IT **528583-46-2P**
(hydrogel with both sensitive thermoresponse and biodegradability)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 24 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:343874 HCA
TITLE: Preparation of amino-substituted camptothecin-PEG derivatives as antitumor agents
PATENT ASSIGNEE(S): Debio Recherche Pharmaceutique S.A., Switz.

SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033525	A1	20030424	WO 2001-IB1912	200110 12

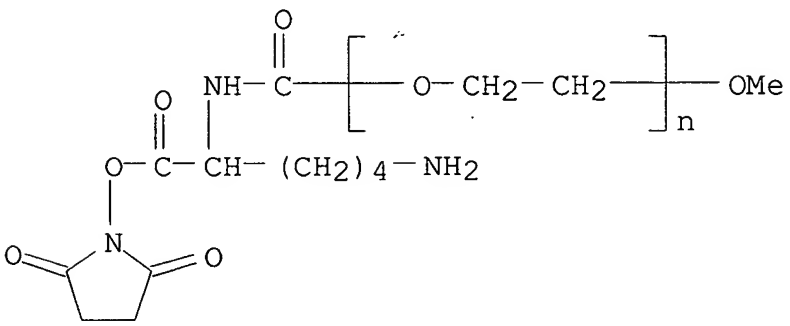
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR
PRIORITY APPLN. INFO.: WO 2001-IB1912 200110 12

AB The present invention relates to a pharmacol. active amino substituted 7-ethylcamptothecin polymer derivative, which has anti-tumor activity and is water-soluble Thus, methoxy PEG-benzotriazolylcarbanate was treated with a tetrapeptide followed by the reaction with 10-amino-7-camptothecin to give the PEG-camptothecin derivative The derivative had antitumor activity against against murine leukemia cells.

IT **511274-90-1**
(in camptothecin-**PEG** derivative **preparation**; **preparation** of amino-substituted camptothecin-**PEG** derivs. as antitumor agents)

RN 511274-90-1 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[(1S)-5-amino-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]pentyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM C07K005-083
ICS C07K005-103; C07K007-06; A61K038-06; A61K038-07; A61K038-08; A61K047-48; A61K035-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 34
IT 7693-46-1, p-Nitrophenyl chloroformate 25322-68-3, Polyethylene glycol 32976-74-2 266313-95-5 **511274-90-1**
(in camptothecin-**PEG** derivative **preparation**; **preparation** of amino-substituted camptothecin-**PEG** derivs. as antitumor agents)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 25 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:326562 HCA
TITLE: Preparation of amino-substituted camptothecin-PEG derivatives as antitumor agents
INVENTOR(S): Veronese, Francesco; Guiotto, Andrea; Sumiya, Hori
PATENT ASSIGNEE(S): Debio Recherche Pharmaceutique S.A., Switz.; Yakult Honsha Co., Ltd.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003031467	A2	20030417	WO 2002-CH562	20021014
WO 2003031467	A3	20030828		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

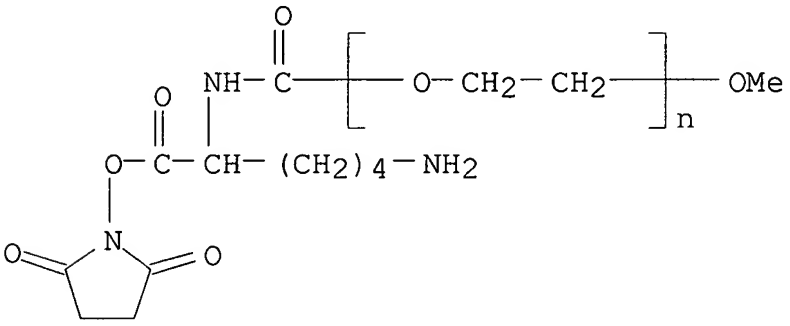
PRIORITY APPLN. INFO.: WO 2002-CH562 200210 14

AB The present invention relates to a pharmacol. active amino-substituted 7-ethylcamptothecin-PEG derivative, which has anti-tumor activity and is water-soluble Thus, methoxy PEG-benzotriazolylcarbanate was treated with a tetrapeptide followed by the reaction with 10-amino-7-camptothecin to give the PEG-camptothecin derivative The derivative had antitumor activity against against murine leukemia cells.

IT **511274-90-1**
(in camptothecin-**PEG** derivative **preparation**; **preparation** of amino-substituted camptothecin-**PEG** derivs. as antitumor agents)

RN 511274-90-1 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[(1S)-5-amino-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]pentyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM C07K005-083
ICS C07K005-103; C07K007-06; A61K038-06; A61K038-07; A61K038-08; A61K047-48; A61P035-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 34

IT 2576-67-2 7693-46-1, p-Nitrophenyl chloroformate 25322-68-3, Polyethylene glycol 32976-74-2 266313-95-5 **511274-90-1** 511274-91-2
(in camptothecin-**PEG** derivative **preparation**; **preparation** of amino-substituted camptothecin-**PEG** derivs. as antitumor agents)

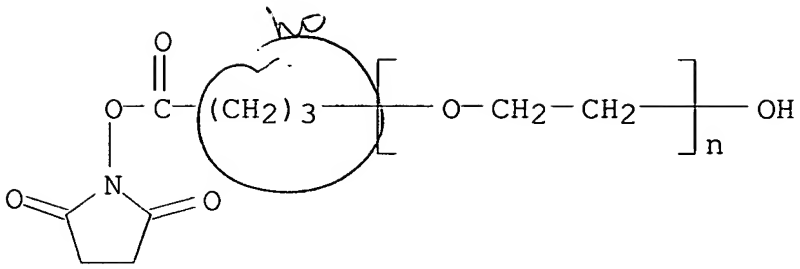
L24 ANSWER 26 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:137765 HCA
TITLE: Heterofunctional polyethylene glycol, and

manufacture
INVENTOR(S): Varshney, Sunil K.; Zhang, Jian Xin
PATENT ASSIGNEE(S): Polymer Source Inc., Can.
SOURCE: U.S. Pat. Appl. Publ., 33 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003027929	A1	20030206	US 2001-895323	20010702
PRIORITY APPLN. INFO.:			US 2001-895323	20010702

AB Heterofunctional polyethylene glycol or polyethylene oxide, formulas RCA2[CH2]n[CH2CH2O]mCH2CH2OH; RCA2O[CH2CH2O]mCH2CH2OH; [HO[CH2CH2O]m[CH2]n]2C(Me)R; [R[CH2]n]2(Me)[OCH2CH2]mOH (where m = 5-10,000; n = 1-20; R = organic substituent, preferably an hydrocarbon substituent that preferably comprises ≥1 heteroatom; A = alkyl, a substituted alkyl or H), and their salts are produced by living anionic polymerization Since the polymerization procedure is a living process, it is possible to tailor the polymer mol. weight from oligomer containing few units (.simeq.5 mer) of ethylene oxide to over 10,000 units of ethylene oxide units. These oligomers or polymers are expected to exhibit excellent biocompatibility, and are also expected to be used as carriers for drug delivery or diagnostic reagents.

IT **196936-07-9P**
(carboxy and hydroxy group-containing **polyethylene glycol**)
RN 196936-07-9 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IC ICM C08F008-00
NCL 525107000
CC 35-7 (Chemistry of Synthetic High Polymers)
IT 9002-92-0P 51160-75-9P 82973-76-0P 164151-96-6P 178206-12-7P
196936-07-9P 493008-34-7P 493008-35-8P 493008-36-9P
(carboxy and hydroxy group-containing **polyethylene glycol**)

L24 ANSWER 27 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:78455 HCA
TITLE: Ointments containing **polyalkylene glycol** derivative-modified biologically active polypeptides
INVENTOR(S): Yamasaki, Motoo; Suzawa, Toshiyuki; Murakami, Tatsuya; Sakurai, Noriko
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000278	A1	20030103	WO 2002-JP6227	20020621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,

SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

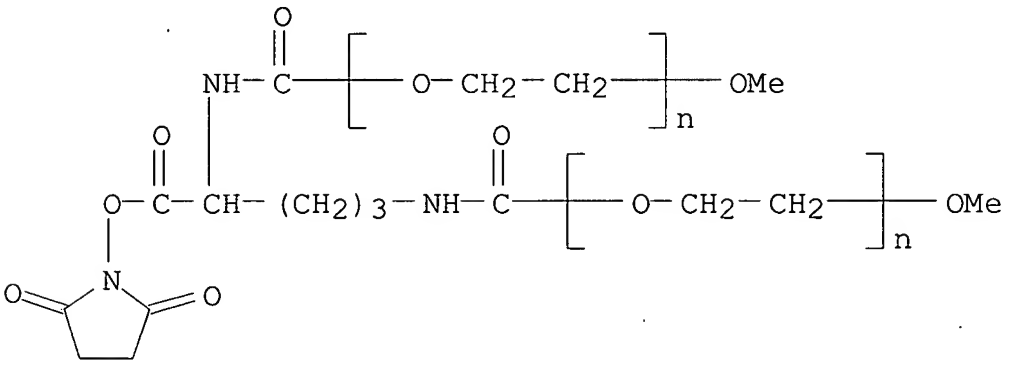
PRIORITY APPLN. INFO.: JP 2001-190330 A 200106 22

AB Disclosed are ointments containing a chemical modified physiol. active polypeptide, wherein the chemical modified physiol. active polypeptide is exemplified by a physiol. active polypeptide chemical modified with at least one **polyalkylene glycol**, and the physiol. active polypeptide to be chemical modified is exemplified by superoxide dismutase, interferon-α, interferon-β, interferon-γ and granulocyte colony-stimulating factor. A polyethylene glycol cyclohexane derivative was prepared, and its N-hydroxysucinimide ester was reacted with recombinant human interferon-β. The modified interferon-β showed excellent antivirus activity in FL cells. Also, an ointment containing modified interferon-β showed improved storage stability as compared with unmodified interferon-β-containing ointment.

IT **479421-84-6DP**, conjugates with polypeptides
(preparation of **polyalkylene glycol** derivative-modified biol. active polypeptides for ointments)

RN 479421-84-6 HCA

CN Poly(oxy-1,2-ethanediyl), α,α'-[[(1S)-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-1,4-butanediyl]bis(iminocarbonyl)]bis[.omega.-methoxy- (9CI) (CA INDEX NAME)



IC ICM A61K038-00
ICS A61K009-06; A61K007-00; A61K007-48; A61K047-30; A61K047-48; A61P043-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 62

ST **polyalkylene glycol** deriv modified polypeptide ointment; polyoxyethylene cyclohexane deriv interferon modification ointment

IT Bone morphogenetic proteins
(7, conjugates with polyoxyalkylene derivs.; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)
IT Proteins
(Klotho, conjugates with polyoxyalkylene derivs.; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)
IT Hepatocyte growth factor
Interleukins
Lactoferrins
Midkines
Stem cell factor
Transforming growth factors
Tumor necrosis factors
(conjugates with polyoxyalkylene derivs.; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)
IT Antibodies and Immunoglobulins
Peptides, biological studies
Polyoxyalkylenes, biological studies
(conjugates; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)
IT Cosmetics
(moisturizers; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)
IT Cosmetics
Human
(ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)
IT Drug delivery systems
(ointments; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)
IT Protein sequences
(**polyalkylene glycol** derivative-modified biol. active polypeptides for ointments)
IT Interferons
(τ, conjugates with polyoxyalkylene derivs.; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)
IT Interferons
(α, conjugates with polyoxyalkylene derivs.; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)
IT Interferons
(β, conjugates with polyoxyalkylene derivs.; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)

IT Interferons
(γ, conjugates with polyoxyalkylene derivs.; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)

IT Interferons
(ω, conjugates with polyoxyalkylene derivs.; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)

IT 481748-38-3
(Unclaimed sequence; preparation of **polyalkylene glycol** derivative-modified biol. active polypeptides for ointments)

IT 481766-88-5
(Unclaimed sequence; preparation of **polyalkylene glycol** derivative-modified biol. active polypeptides for ointments)

IT 481748-39-4DP, conjugates with polyoxyalkylene derivs.
481748-40-7DP, conjugates with polyoxyalkylene derivs.
(amino acid sequence; preparation of **polyalkylene glycol** derivative-modified biol. active polypeptides for ointments)

IT 9054-89-1DP, conjugates with polyoxyalkylene derivs.
(copper-zinc-containing; ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)

IT 292819-64-8DP, KM 871, conjugates with polyoxyalkylene derivs.
(ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)

IT 9000-96-8D, Arginase, conjugates with polyoxyalkylene derivs.
9001-47-2D, Glutaminase, conjugates with polyoxyalkylene derivs.
9001-90-5D, Plasmin, conjugates with polyoxyalkylene derivs.
9001-91-6D, Plasminogen, conjugates with polyoxyalkylene derivs.
9002-01-1D, Streptokinase, conjugates with polyoxyalkylene derivs.
9002-12-4D, Uricase, conjugates with polyoxyalkylene derivs.
9002-64-6D, Parathyroid hormone, conjugates with polyoxyalkylene derivs. 9007-12-9D, Calcitonin, conjugates with polyoxyalkylene derivs. 9007-92-5D, Glucagon, conjugates with polyoxyalkylene derivs. 9014-42-0D, Thrombopoietin, conjugates with polyoxyalkylene derivs. 9015-68-3D, Asparaginase, conjugates with polyoxyalkylene derivs. 9026-93-1D, Adenosine deaminase, conjugates with polyoxyalkylene derivs. 9088-07-7D, Natriuretic peptide, conjugates with polyoxyalkylene derivs. 11096-26-7D, Erythropoietin, conjugates with polyoxyalkylene derivs.
62031-54-3D, Fibroblast growth factor, conjugates with polyoxyalkylene derivs. 62229-50-9D, Epidermal growth factor, conjugates with polyoxyalkylene derivs. 67763-96-6D, Insulin-like growth factor 1, conjugates with polyoxyalkylene derivs.
86090-08-6D, Angiostatin, conjugates with polyoxyalkylene derivs.
96352-57-7D, Glucagon like peptide, conjugates with polyoxyalkylene

derivs. 105913-11-9D, Plasminogen activator, conjugates with polyoxyalkylene derivs. 106602-62-4D, Amylin, conjugates with polyoxyalkylene derivs. 127464-60-2D, Vascular endothelial growth factor, conjugates with polyoxyalkylene derivs. 143011-72-7D, Granulocyte colony stimulating factor, conjugates with polyoxyalkylene derivs. 169494-85-3D, Leptin, conjugates with polyoxyalkylene derivs. 187888-07-9D, Endostatin, conjugates with polyoxyalkylene derivs. 250740-90-0D, Angiopoietin, conjugates with polyoxyalkylene derivs.
(ointments containing **polyalkylene glycol** derivative-modified biol. active polypeptides)

IT 56-12-2, γ-Aminobutyric acid, reactions 77-95-2 78-90-0, Propylene diamine 108-77-0, Cyanuric chloride 109-76-2, 1,3-Diaminopropane 115-77-5, Pentaerythritol, reactions 138-59-0, Shikimic acid 541-41-3, Ethoxycarbonyl chloride 541-59-3, Maleimide 604-68-2, α-D-Glucose pentaacetate 5704-04-1, Tricine 6346-09-4 9004-74-4, Methoxypolyethylene glycol 16526-68-4 20724-48-5, Ornithine hydrochloride 36255-44-4, 3-Bromopropionaldehyde dimethylacetal 54897-59-5, 2,3-Diaminopropionic acid hydrochloride 60662-54-6 71782-42-8 74124-79-1, N,N'-Disuccinimidyl carbonate 152967-61-8 154932-88-4 166039-68-5
(preparation of **polyalkylene glycol** derivative-modified biol. active polypeptides for ointments)

IT 54631-96-8P 55750-49-7P, N-Ethoxycarbonyl maleimide 58320-73-3P 67665-18-3P 72708-10-2P 72890-46-1P 74808-10-9P, α-D-Glucopyranose-2,3,4,6-tetraacetate-1-(2,2,2-trichloroethanimidate) 92450-98-1P 107383-91-5P 134141-55-2P 135649-01-3P 180915-61-1P 185115-32-6P 280766-92-9P 280766-93-0P 348098-33-9P 348098-42-0P 445389-25-3P 445389-27-5P 445389-29-7P 445389-33-3P 445389-36-6P 445389-37-7P 445389-41-3P 479421-70-0P 479421-71-1P 479421-73-3P 479421-76-6P 479421-80-2P 479421-81-3P 479421-82-4P 479421-85-7P 479421-87-9P 479421-91-5P 479421-92-6P 479421-93-7P 479421-94-8P 481678-15-3P 481678-18-6P 481678-22-2P 481678-27-7P 481678-32-4P 481678-34-6P
(preparation of **polyalkylene glycol** derivative-modified biol. active polypeptides for ointments)

IT 72708-10-2DP, conjugates with polypeptides 92451-01-9DP, conjugates with polypeptides 99126-64-4DP, conjugates with polypeptides 174569-25-6DP, conjugates with polypeptides 280766-93-0DP, conjugates with polypeptides 445389-35-5DP, conjugates with polypeptides 445389-35-5P 445389-36-6DP, conjugates with polypeptides 445389-37-7DP, conjugates with polypeptides 479421-70-0DP, conjugates with polypeptides 479421-72-2DP, conjugates with polypeptides 479421-74-4DP, conjugates with polypeptides 479421-75-5DP, conjugates with

polypeptides 479421-77-7DP, conjugates with polypeptides 479421-78-8DP, conjugates with polypeptides 479421-79-9DP, conjugates with polypeptides 479421-80-2DP, conjugates with polypeptides 479421-81-3DP, conjugates with polypeptides 479421-83-5DP, conjugates with polypeptides **479421-84-6DP**, conjugates with polypeptides **479421-86-8DP**, conjugates with polypeptides 479421-88-0DP, conjugates with polypeptides 479421-89-1DP, conjugates with polypeptides **479421-90-4DP**, conjugates with polypeptides 479421-91-5DP, conjugates with polypeptides 481678-15-3DP, conjugates with polypeptides 481678-18-6DP, conjugates with polypeptides 481678-22-2DP, conjugates with polypeptides 481678-30-2DP, conjugates with polypeptides
(preparation of **polyalkylene glycol** derivative-modified biol. active polypeptides for ointments)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

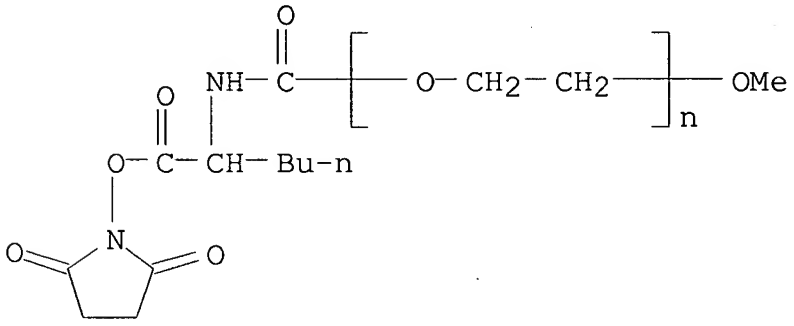
L24 ANSWER 28 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:61241 HCA
TITLE: Selective Alkylation and Acylation of α and ε Amino Groups with PEG in a Somatostatin Analogue: Tailored Chemistry for Optimized Bioconjugates
AUTHOR(S): Morpurgo, Margherita; Monfardini, Cristina; Hofland, Leo J.; Sergi, Mauro; Orsolini, Paolo; Dumont, Jean M.; Veronese, Francesco M.
CORPORATE SOURCE: Dipartimento Scienze Farmaceutiche, Universita degli Studi di Padova, Padua, 35131, Italy
SOURCE: Bioconjugate Chemistry (2002), 13(6), 1238-1243 CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of the type and location of polymer grafting on the biol. activity of different mono-PEG derivs. of the somatostatin analog RC160 were evaluated. A chemical strategy to obtain mono-PEG alkylation or acylation of the peptide's α-terminal or lysyl-ε primary amines was devised. Selective BOC protection of the two available primary amines, followed by reaction with two different PEG reagents and removal of the protecting group, was carried out. Chemical characterization, structural studies, and the evaluation of the biol. activity of the bioconjugates synthesized allowed the identification of the one having characteristics more suitable for therapeutic application. This corresponds to the mono-ε-lysyl-PEGylated form, obtained by reductive alkylation, where the amine pos. charge is preserved. The

results suggest the importance of preliminary studies in the development of new polymer-peptide conjugates with improved pharmacol. properties.

IT **136372-28-6**
(alkylation and acylation of somatostatin analog (RC 160) with **PEG** in bioconjugates **preparation**)

RN 136372-28-6 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[(1S)-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]pentyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 2, 34, 37

IT 70086-22-5 **136372-28-6**
(alkylation and acylation of somatostatin analog (RC 160) with **PEG** in bioconjugates **preparation**)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 29 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 137:389096 HCA

TITLE: Preparation and properties of alginate lyase modified with poly(ethylene glycol)

AUTHOR(S): Sakakibara, Hiroyuki; Tamura, Takashi; Suzuki, Takehiko; Hisano, Tomohiro; Abe, Shiro; Murata, Kousaku

CORPORATE SOURCE: DDS Research Department, Discovery Research Laboratory, Tanabe Seiyaku Company, Ltd., Osaka, 532-8505, Japan

SOURCE: Journal of Pharmaceutical Sciences (2002), 91(4), 1191-1199
CODEN: JPMSAE; ISSN: 0022-3549

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

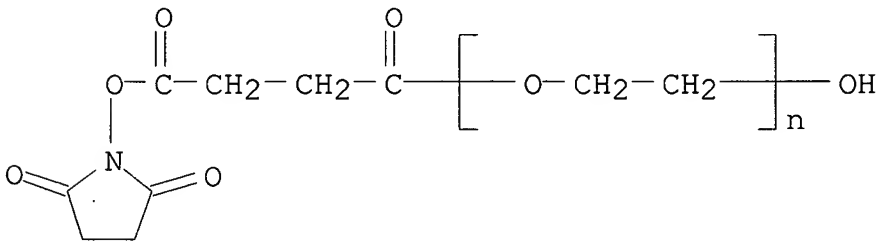
LANGUAGE: English

AB Modification of the enzyme alginate lyase (AL) with poly(ethylene glycol) (PEG) was attempted for the degradation and removal of alginate biofilms in infectious diseases. The modification of AL with PEG was attempted with three kinds of N-succinimidyl succinate PEG (SS-PEG), which differed in mol. weight (i.e., 2000, 5000 and 12,000 Da). The conjugation of PEG to free amino groups on AL was confirmed by gel permeation chromatog. Quantification of residual free amino groups revealed that PEG modification progressed further with a higher pH and a larger molar ratio of SS-PEG to AL. The reproducibility of the reaction was fairly good. The enzyme activity decreased with increasing PEG modification but the immunoreactivity toward anti-AL antibodies, as evaluated by an ELISA method, was much more remarkably reduced. The immunoreactivity was more reduced by the conjugated PEG with the larger mol. weight In the reaction with PEG of mol. weight 12,000 Da, we obtained PEG-modified AL retaining .apprx.40% enzyme activity but only 0.5% of the immunoreactivity of native AL.

IT **102743-95-3DP**, alginate lyase conjugate
(**PEG**-conjugated alginate lyase for removal of biofilms in infectious diseases)

RN 102743-95-3 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1

IT 9024-15-1DP, Alginate lyase, poly(ethylene glycol) conjugate
25322-68-3DP, Poly(ethylene glycol), alginate lyase conjugate
102743-95-3DP, alginate lyase conjugate
(**PEG**-conjugated alginate lyase for removal of biofilms in infectious diseases)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 30 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:329336 HCA

TITLE: PEG grafted polylysine with fusogenic peptide for gene delivery: high transfection efficiency with low cytotoxicity

AUTHOR(S): Lee, Haeshin; Jeong, Ji Hoon; Park, Tae Gwan
CORPORATE SOURCE: Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Yusong-gu, Taejon, 305-701, S. Korea

SOURCE: Journal of Controlled Release (2002), 79(1-3), 283-291
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB For efficient gene delivery into cells, a new formulation method based on using polyethylene glycol (PEG) grafted poly(L-lysine) (PLL) and a fusogenic peptide is presented in this study. First, PEG grafted PLL (PEG-g-PLL) was complexed with DNA by controlling the polymer/DNA ratio to form neg. charged nano-particulate complexes. A pos. charged fusogenic peptide, KALA, was then coated by ionic interaction onto the surface of polymer/DNA complexes to make net pos. charged KALA/polymer/DNA complexes. The use of PEG-g-PLL for KALA coating significantly suppressed the aggregation of complexes due to steric stabilization effect of PEG present on the surface, while the use of PLL alone induced severe aggregation of the complexes via KALA mediated inter-particulate crosslinking. For PEG-g-PLL/DNA complexes, enhanced transfection efficiency was observed with increasing amount of KALA. This suggests that maintaining the size of DNA/polymer complexes after KALA coating plays an important role in gene transfection. KALA/DNA/PEG-g-PLL complexes exhibited lower cytotoxicity compared with other polymer/DNA complexes.

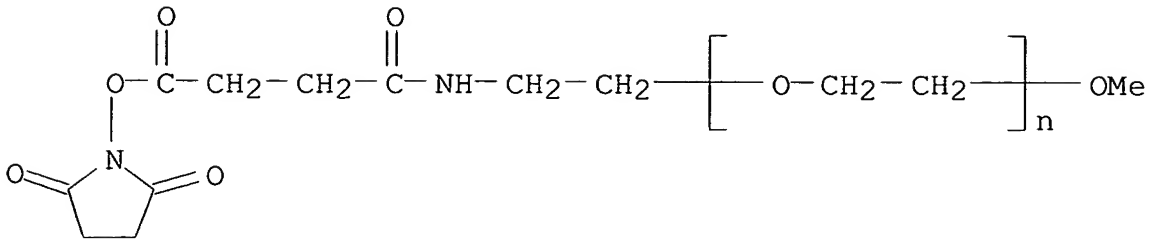
IT **473798-34-4DP**, DNA complex
(**PEG** grafted polylysine with fusogenic peptide for gene delivery with high transfection efficiency with low cytotoxicity)

RN 473798-34-4 HCA

CN L-Lysine, polymer with α-[2-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]amino]ethyl]-ω-methoxypoly(oxy-1,2-ethanediyl), graft (9CI) (CA INDEX NAME)

CM 1

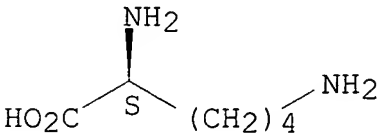
CRN 92451-00-8
CMF (C2 H4 O)n C11 H16 N2 O6
CCI PMS



CM 2

CRN 56-87-1
CMF C6 H14 N2 O2

Absolute stereochemistry.

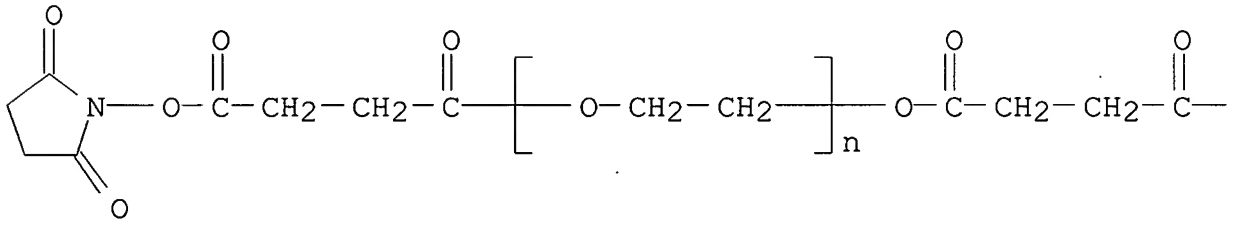


CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 35
IT **473798-34-4DP**, DNA complex
(**PEG** grafted polylysine with fusogenic peptide for gene delivery with high transfection efficiency with low cytotoxicity)
IT **473798-34-4P**
(**PEG** grafted polylysine with fusogenic peptide for gene delivery with high transfection efficiency with low cytotoxicity)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

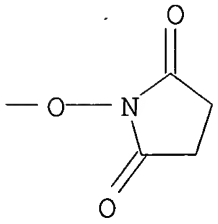
L24 ANSWER 31 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:299719 HCA
TITLE: Synthesis of water-soluble taxol prodrugs bonded with PEG
AUTHOR(S): Li, Jin-liang; Feng, Xia; Liu, Bin; Yuan, Ying-jin
CORPORATE SOURCE: School of Chemical Engineering and Technology, Tianjin University, Tianjin, 300072, Peop. Rep. China
SOURCE: Tianjin Daxue Xuebao, Ziran Kexue Yu Gongcheng Jishuban (2001), 34(6), 808-811
CODEN: TDXZAE

PUBLISHER: Tianjin Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Succinic acids and amino acids were introduced into the mol. skeleton of Polyethylene glycol (PEG) through functionalization to give PEG-DA-AA. Esterification of 2'-OH of taxol with different PEG-DA-AA produced a series of water-soluble taxol derivs.
IT **85419-94-9P**
(synthesis of water-soluble taxol prodrugs bonded with **PEG**)
RN 85419-94-9 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



CC 63-5 (Pharmaceuticals)
IT 37684-51-8P **85419-94-9P** 468066-16-2P 468066-17-3P 468066-18-4P 468066-19-5P 468066-20-8P
(synthesis of water-soluble taxol prodrugs bonded with **PEG**)

L24 ANSWER 32 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:174894 HCA
TITLE: PEG-conjugates of HGF-NK4
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 25 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1234583	A1	20020828	EP 2001-104640	20010223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2438308	AA	20020926	CA 2002-2438308	20020221
WO 2002074344	A2	20020926	WO 2002-EP1837	20020221
WO 2002074344	A3	20031204		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
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US 2003012775	A1	20030116	US 2002-81309	20020221
EP 1389132	A2	20040218	EP 2002-700263	20020221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004521139	T2	20040715	JP 2002-573051	20020221
BR 2002007510	A	20040727	BR 2002-7510	20020221
NO 2003003737	A	20031021	NO 2003-3737	20030822

PRIORITY APPLN. INFO.: EP 2001-104640 A 200102 23

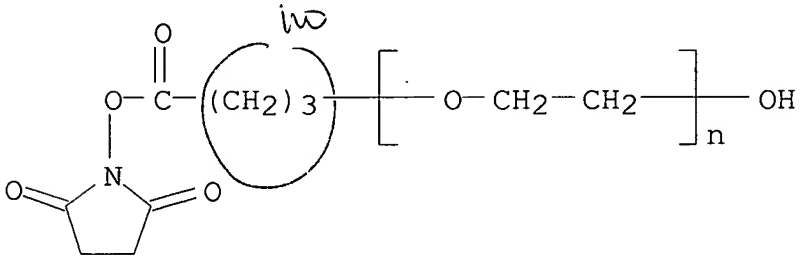
WO 2002-EP1837 W 200202 21

AB A conjugate comprising an N-terminal fragment of hepatocyte growth factor (HGF/SF) consisting of the hairpin domain and the four kringle regions of the α-chain and one to three polyethylene glycol group(s), said polyethylene glycol group(s) having an overall mol. weight of from about 10 to 40 kDa, has improved properties and is a useful therapeutic agent for tumor treatment.

IT **196936-07-9DP**, conjugates
(**PEG**-conjugates of HGF-NK4 for antitumor use)

RN 196936-07-9 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IC ICM A61K047-48
ICS A61P035-00

CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1

IT 123502-58-9DP, conjugates **196936-07-9DP**, conjugates
(**PEG**-conjugates of HGF-NK4 for antitumor use)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 33 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 137:159313 HCA

TITLE: Polymer conjugates of neublastin for therapeutic and diagnostic application

INVENTOR(S): Sah, Dinah W. Y.; Pepinsky, R. Blake; Borjack-Sjodin, Paula Ann; Miller, Stephan S.; Rossomando, Anthony

PATENT ASSIGNEE(S): Biogen, Inc., USA

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060929	A2	20020808	WO 2002-US2319	20020125
WO 2002060929	A3	20030306		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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CA 2436407	AA	20020808	CA 2002-2436407	20020125
EE 200300355	A	20031015	EE 2003-355	20020125
EP 1355936	A2	20031029	EP 2002-714792	20020125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2003003441	A	20031001	NO 2003-3441	20030801
WO 2004069176	A2	20040819	WO 2004-US2763	20040202
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				

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PRIORITY APPLN. INFO.:

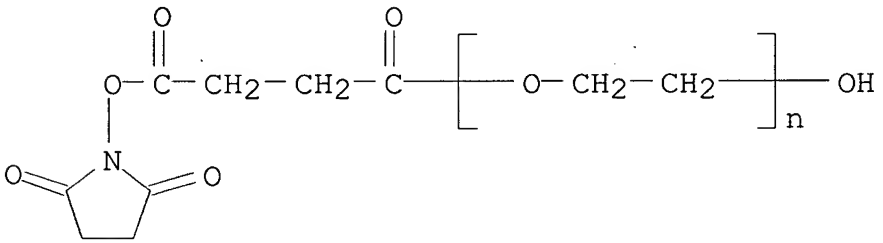
US 2001-266071P	P	20010201
WO 2002-US2319	W	20020125
US 2003-356264	A1	20030131

AB A variant neublastin polypeptide suitable for formation of a conjugate comprising the variant neublastin polypeptide coupled to a polymer containing a **polyalkylene glycol** moiety is disclosed. The present conjugate has prolonged bioavailability and, in preferred embodiments, prolonged biol. activity relative to non-modified or wild-type forms of neublastin. The conjugates of the invention are usefully employed in therapeutic as well as non-therapeutic, e.g., diagnostic, applications.

IT **102743-95-3D**, conjugates
(polymer conjugates of neublastin for therapeutic and diagnostic application)

RN 102743-95-3 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IC ICM C07K014-00

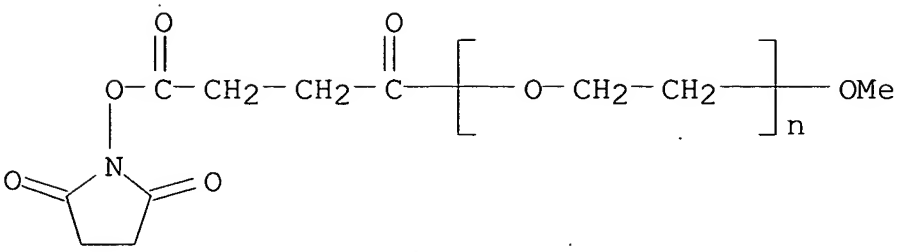
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1

IT 6066-82-6 **102743-95-3D**, conjugates 123502-58-9D, conjugates **196936-07-9D**, conjugates
(polymer conjugates of neublastin for therapeutic and diagnostic application)

L24 ANSWER 34 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:136655 HCA
TITLE: Biophysical consequences of linker chemistry and polymer size on stealth erythrocytes: size does matter
AUTHOR(S): Bradley, Amanda J.; Murad, Kari L.; Regan, Katy L.; Scott, Mark D.
CORPORATE SOURCE: Albany Medical College, Center for Immunology and Microbial Disease, Albany, NY, USA
SOURCE: Biochimica et Biophysica Acta (2002), 1561(2), 147-158
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Immunocamouflaged red blood cells (RBC) are produced by cell surface derivatization with methoxypolyethylene glycol (mPEG). These immunol. attenuated cells may reduce the risk of allosensitization in chronically transfused patients. To characterize the effects of differing linker chemistries and polymer lengths, RBC were modified with cyanuric chloride activated mPEG (C-mPEG 5 kDa), benzotriazole carbonate methoxyPEG (BTC-mPEG; 5 or 20 kDa) or N-**hydroxysuccinimidyl** ester of mPEG propionic acid (SPA-mPEG; 2, 5 or 20 kDa). Biophys. methods including particle electrophoresis and aqueous two-phase polymer partitioning were employed to compare the **PEG** derivs. While C-mPEG was faster reacting, both BTC-mPEG and SPA-mPEG gave comparable findings after 1 h. Both **PEG** surface d. and mol. mass had a large effect on RBC surface properties. Proportional changes in electrophoretic mobility and preferential phase partitioning were achieved by increasing either the quantity of surface **PEG** or the **PEG** mol. mass. In addition, two-phase partitioning may provide a means for efficiently removing unmodified or lightly modified (hence potentially immunogenic) RBC in the clin. setting. Furthermore, mPEG modification significantly inhibits cell-cell interaction as evidenced by loss of Rouleaux formation and, consequently, sedimentation rate. Importantly, BTC-mPEG 20 kDa RBC showed normal in vivo survival in mice at immunoprotective concns. (up to 2 mM).

IT **78274-32-5**
(biophys. consequences of linker chemical and polymer size on stealth erythrocytes: size does matter)
RN 78274-32-5 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 6-7 (General Biochemistry)
Section cross-reference(s): 1, 13
IT 63464-05-1 **78274-32-5** 266313-95-5
(biophys. consequences of linker chemical and polymer size on stealth erythrocytes: size does matter)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 35 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:63650 HCA
TITLE: Synthesis of high molecular weight non-peptidic polymer derivatives, their preparation and their conjugates with biologically active molecules
INVENTOR(S): Kozlowski, Antoni; Shen, Xiaoming; Bentley, Michael David; Fang, Zhihao
PATENT ASSIGNEE(S): Shearwater Corporation, USA; Nektar Therapeutics AL, Corp.
SOURCE: U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002082345	A1	20020627	US 2001-24357	20011218
US 6774180	B2	20040810		
CA 2431977	AA	20020801	CA 2001-2431977	20011218
WO 2002059179	A2	20020801	WO 2001-US49081	20011218
WO 2002059179	A3	20021003		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

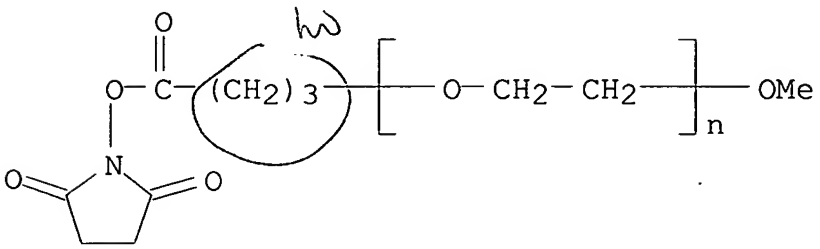
EP 1345982	A2	20030924	EP 2001-994295 200112 18
			R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004525212	T2	20040819	JP 2002-559475 200112 18
US 2004236015	A1	20041125	US 2003-734858 200312 11

PRIORITY APPLN. INFO.:	US 2000-256801P	P 200012 18
	US 2001-24357	A2 200112 18
	WO 2001-US49081	W 200112 18

AB The title polymers such as high mol. weight derivs. of activated poly(ethylene glycol) and the like polymers are prepared in high purity by conjugating a large PEG mol. to a small PEG mol. Most of the reaction steps can be accomplished on the more readily purified small mol. to avoid laborious purification of the high mol. weight derivs.
Monomethoxypoly(ethylene glycol) maleimide was prepared by reaction of monomethoxypoly(ethylene glycol) benzotriazole carbonate with maleimido-triethyleneglycol-amine trifluoroacetate in the presence of catalyst at room temperature

IT **187848-51-7P**
(**polyethylene glycol** derivs. for conjugates with biol. active mols.)
RN 187848-51-7 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM C08L063-10
ICS C07H021-04
NCL 525054200
CC 35-8 (Chemistry of Synthetic High Polymers)
IT 9041-92-3DP, reaction product with polyethylene glycol derivs.
32130-27-1P 99126-64-4P 125061-88-3P 174569-25-6P
187848-51-7P 439590-71-3P
(**polyethylene glycol** derivs. for conjugates with biol. active mols.)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 36 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:48103 HCA
TITLE: Preparation of self-organized micro-patterned polymer films having cell adhesive ligands
AUTHOR(S): Nishida, Jin; Nishikawa, Kazutaka; Nishimura, Shin-Ichiro; Wada, Shigeo; Karino, Takeshi; Nishikawa, Takehiro; Ijiro, Kuniharu; Shimomura, Masatsugu
CORPORATE SOURCE: Research Institute for Electronic Science, Hokkaido University, Sapporo, 060-0812, Japan
SOURCE: Polymer Journal (Tokyo, Japan) (2002), 34(3), 166-174
CODEN: POLJB8; ISSN: 0032-3896
PUBLISHER: Society of Polymer Science, Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This article describes novel three methods for micro-patterning of cell adhesive ligands by using the self-organized honeycomb-patterned structure formed by the simple cast method. A first method is a direct preparation of a patterned film by casting an amphiphilic polymer containing lactose residue which is one of cell adhesive ligands. A benzene solution of the amphiphilic polymer was cast at high humidity on a glass substrate. Atomic force microscopy

(AFM) observation of the film showed that a honeycomb pattern with microporousness with as large as micrometer size in diameter was formed. The film was immersed into an aqueous fluorescence-labeled lectin solution to investigate the distribution of lactoses on the patterned film. Consistence of a fluorescence image of the lectin bound film with the honeycomb pattern showed that the lactose residues were existed not at the holes but at the rims of the honeycomb-patterned film. A second method is to immobilize gelatin, which is one also one of cell adhesive ligands, on the honeycomb-patterned film by chemical reaction. A honeycomb-patterned film was prepared from chloroform solution of an amphiphilic polymer containing reactive succinimide ester groups, and then the film was immersed into an aqueous fluorescence-labeled gelatin solution to introduce gelatin on the film surface. Immobilization of gelatin onto honeycomb-patterned film was confirmed by the fluorescence microscope. A third method is another way to introduce gelatin onto the honeycomb film by the specific avidin-biotin interaction. A honeycomb-patterned film was prepared from amphiphilic polymer containing biotin residues and dodecyl groups, and then the film was immersed into a avidin solution and a biotinylated fluorescence labeled gelatin solution successively. By the fluorescence microscopic observation of the film, gelatin was confirmed to be immobilized at the rims of the honeycomb pattern via the avidin-biotin interaction. Cell culture was performed on the gelatin immobilized patterned film prepared by second method. Bioactivity of gelatin immobilized honeycomb-patterned film was confirmed by adhesion of cell onto the film.

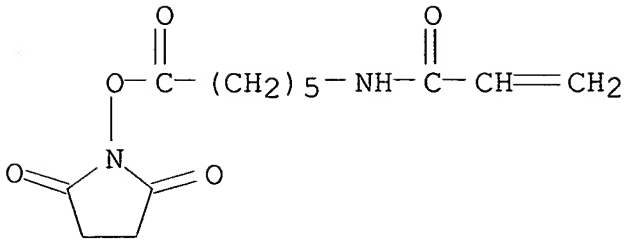
IT **438544-69-5DP**, reaction products with biotin derivs.
(methods for preparation of self-organized micro-patterned polymer films having cell adhesive ligands and their structural characteristics and bioactivities)

RN 438544-69-5 HCA

CN 2-Propenamide, N-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-, polymer with N-dodecyl-2-propenamide (9CI) (CA INDEX NAME)

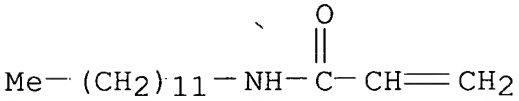
CM 1

CRN 63392-86-9
CMF C13 H18 N2 O5



CM 2

CRN 1506-53-2
CMF C15 H29 N O



CC 38-3 (Plastics Fabrication and Uses)
Section cross-reference(s): 6, 35, 37
IT 66640-86-6DP, reaction products with N-dodecylacrylamide-N-**hydroxysuccinimidyl** 6-acrylamidohexanoate copolymer
72040-63-2DP, reaction products with gelatin 256239-34-6P
258337-40-5P, 6-Acrylamidohexanoic acid-N-dodecylacrylamide copolymer **438544-69-5DP**, reaction products with biotin derivs. **438544-69-5P**, N-Dodecylacrylamide-N-**hydroxysuccinimidyl** 6-acrylamidohexanoate copolymer
(methods for preparation of self-organized micro-patterned polymer films having cell adhesive ligands and their structural characteristics and bioactivities)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 37 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:374762 HCA
TITLE: A tissue sealant based on reactive multifunctional polyethylene glycol
AUTHOR(S): Wallace, D. G.; Cruise, G. M.; Rhee, W. M.; Schroeder, J. A.; Prior, J. J.; Ju, J.; Maroney, M.; Duronio, J.; Ngo, M. H.; Estridge, T.; Coker, G. C.
CORPORATE SOURCE: Cohesion Technologies, Palo Alto, CA, 94303, USA
SOURCE: Journal of Biomedical Materials Research (2001), 58(5), 545-555

CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

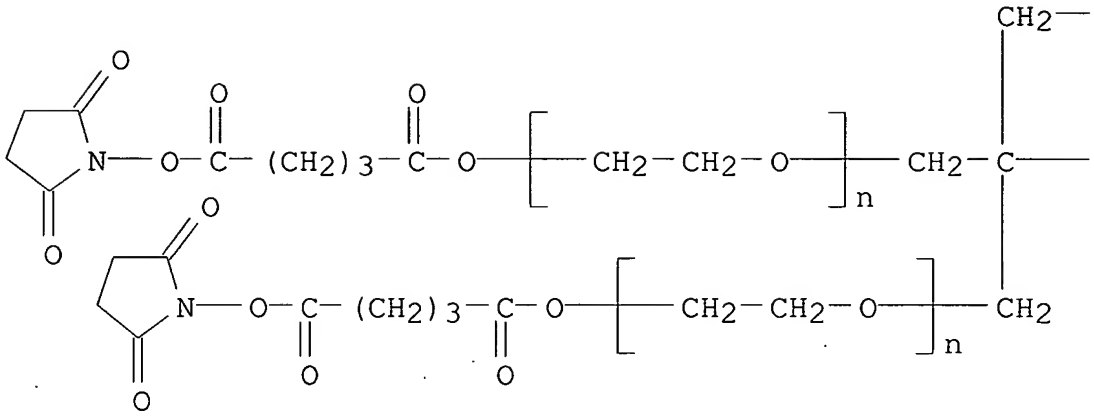
AB A rapidly gelling synthetic tissue sealant was developed from tetra-succinimidyl and tetra-thiol-derivatized polyethylene glycol (PEG). The two reagents were dissolved in aqueous buffers at 20% (w/v) solids and sprayed on the tissue site, with the use of a sprayer/mixer device. Good adhesion to collagen membranes, PTFE grafts, and carotid artery was observed in vitro. In a burst test on collagen membranes with a 2-mm orifice defect, the gel sustained fluid pressures of 125±36 mm Hg (n = 18), fivefold greater than capillary blood pressure and one-half that observed in hypertension. On 0.4-mm-diameter puncture defects in PTFE grafts, pressures of 390-490 mm Hg were sustained, and on 0.6-0.9-mm puncture defects in carotid arteries, pressures of 490 to 840 mm Hg were sustained. In vitro data corresponded to results in vivo, where bleeding in rabbit arteries was stopped immediately in five out of six trials. A significant reduction in time to hemostasis and blood loss, compared to controls, was observed Carotid artery and s.c. implant data in rabbits showed that the formula was compatible with biol. tissue. Rapid gelling and effective sealing were dependent on the presence of active succinimidyl ester and thiol groups on PEG. HPLC and chemical substitution methods were useful in predicting whether batches of derivatized PEG would perform satisfactorily.

IT **302781-03-9P**
(tissue sealant based on reactive multifunctional **polyethylene glycol**)

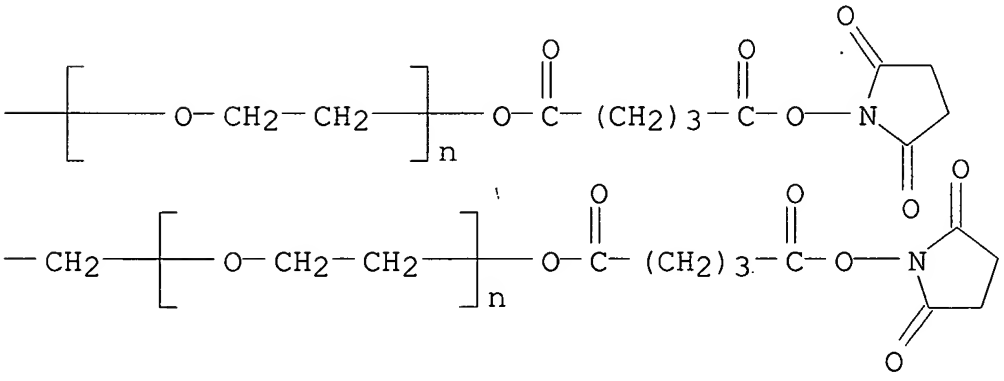
RN 302781-03-9 HCA

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-[[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]oxy]-, ether with 2,2-bis(hydroxymethyl)-1,3-propanediol (4:1) (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



CC 63-7 (Pharmaceuticals)
IT 188492-68-4P **302781-03-9P**
(tissue sealant based on reactive multifunctional **polyethylene glycol**)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 38 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:345630 HCA

TITLE: Enhancing transfection efficiency using polyethylene glycol grafted polyethylenimine and fusogenic peptide

AUTHOR(S): Lee, Haeshin; Jeong, Ji Hoon; Lee, Je Hoon; Park, Tae Gwan

CORPORATE SOURCE: Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Taejon, 305-701, S. Korea

SOURCE: Biotechnology and Bioprocess Engineering (2001), 6(4), 269-273
CODEN: BBEIAU; ISSN: 1226-8372

PUBLISHER: Korean Society for Biotechnology and Bioengineering

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study presents a new formulation method for improving DNA transfection efficiency using a fusogenic peptide and polyethylene glycol grafted polyethylenimine. Succinimidyl succinate polyethylene glycol (PEG-SSA) was conjugated with polyethylenimine (PEI). PEI is well known for a good endosomal escaping and DNA condensing agent. The pos. charged synthetic fusogenic peptide, KALA, was coated on the neg. charged PEG-g-PEI/DNA and PEI/DNA complexes. The KALA/PEI/DNA complexes exhibited aggregation behavior at higher KALA coating amts. with an effective diameter of around 1,000 nm. However, the KALA/PEG-g-PEI/DNA complexes were 100-300 nm in size with a surface zeta-potential (ζ) value of about +20 mV. The conjugated PEG mols. suppressed any KALA-mediated inter-particle aggregation, and thereby improved the transfection efficiency. Consequently, the transfection efficiency of the KALA/PEG-g-PEI/DNA complexes was obtained by utilizing both the fusogenic activity of KALA and the steric repulsion effect of PEG.

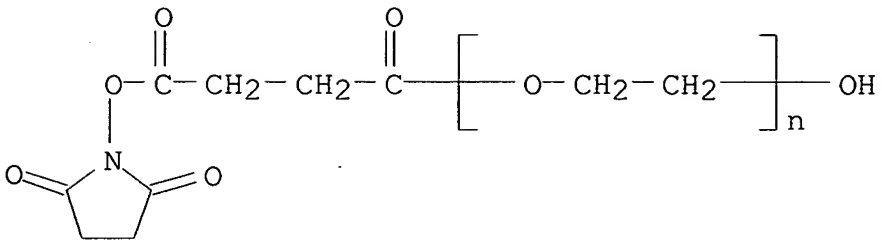
IT **417725-30-5P**
(enhancing transfection efficiency using **polyethylene glycol** grafted polyethylenimine and fusogenic peptide)

RN 417725-30-5 HCA

CN Aziridine, polymer with α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-hydroxypoly(oxy-1,2-ethanediyl), graft (9CI) (CA INDEX NAME)

CM 1

CRN 102743-95-3
CMF (C2 H4 O)n C8 H9 N O6
CCI PMS



CM 2

CRN 151-56-4
CMF C2 H5 N

CC 63-5 (Pharmaceuticals)
IT **417725-30-5P**
(enhancing transfection efficiency using **polyethylene glycol** grafted polyethylenimine and fusogenic peptide)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 39 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:172754 HCA
TITLE: Highly reactive branched polymer and proteins or peptides conjugated with the polymer
INVENTOR(S): Park, Myung-Ok; Lee, Kang-Choon; Cho, Sung-hHe
PATENT ASSIGNEE(S): S. Korea
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009766	A1	20020207	WO 2001-KR1209	200107 13

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

KR 2002010363 A 20020204 KR 2000-44046 200007 29

PRIORITY APPLN. INFO.: KR 2000-44046 A 200007 29

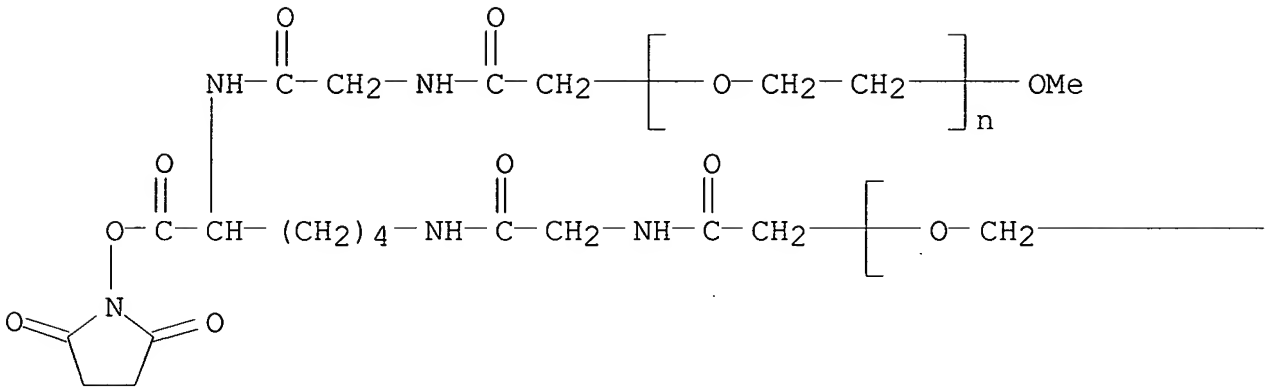
AB The present invention relates to new biocompatible polymer derivs., and a protein-polymer or a peptide-polymer which is produced by conjugation of biol. active protein and peptide with the biocompatible polymer derivs. More particularly, the present invention relates to a highly reactive branched biocompatible polymer derivative containing a long linker between polymer derivs. and protein or peptide mols., which is minimized in decrease the biol. activity of proteins by conjugating the less number of polymer derivs. to the active sites of proteins, improved in water solubility, and protected from being degraded by protease. In hence, the highly reactive branched biocompatible polymer-proteins or peptides conjugates with long linker retain the biol. activity for a long period of time and improve a bioavailability of bioactive proteins and peptides. For example, activated **PEG**-interferon conjugates were prepared by adding 3 mg of succinic N-**hydroxysuccinimidyl** di-**PEG** to 3 mg of interferon in 0.1 M phosphate buffer solution, pH 7.0 at ambient temperature The reaction was stopped with 0.1 M glycine and the excess reagents were using Centricon-30.

IT **395645-02-0DP**, conjugates with peptides or proteins (highly reactive branched polymers and their conjugates with proteins or peptides)

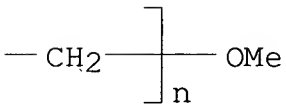
RN 395645-02-0 HCA

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-methoxy-, diether with 1-[[N2,N6-bis[N-(hydroxyacetyl)glycyl]-L-lysyl]oxy]-2,5-pyrrolidinedione (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IC ICM A61K047-48
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 2, 7, 15, 37
IT 9000-96-8DP, Arginase, polymer conjugates 9001-05-2DP, Catalase, polymer conjugates 9001-25-6DP, Blood-coagulation factor VII, polymer conjugates 9001-28-9DP, Factor IX, polymer conjugates 9001-34-7DP, Galactosidase, polymer conjugates 9001-37-0DP, Glucose oxidase, polymer conjugates 9001-45-0DP, Glucuronidase, polymer conjugates 9001-62-1DP, Lipase, polymer conjugates 9002-10-2DP, Tyrosinase, polymer conjugates 9002-12-4DP, Uricase, polymer conjugates 9002-64-6DP, Parathyroid hormone, polymer conjugates 9002-71-5DP, Thyroid stimulating hormone, polymer conjugates 9002-72-6DP, Growth hormone, conjugates with **PEG** derivative 9002-72-6DP, Somatotropin, polymer conjugates 9002-89-5DP, Polyvinyl alcohol, conjugates with peptides or proteins 9003-01-4DP, Polyacrylic acid, conjugates with peptides or proteins 9003-05-8DP, Polyacrylamide, conjugates with peptides or proteins 9004-07-3DP, Chymotrypsin, polymer conjugates 9004-10-8DP, Insulin, polymer conjugates 9004-54-0DP, Dextran, conjugates with

peptides or proteins 9007-12-9DP, Calcitonin, polymer conjugates 9015-68-3DP, Asparaginase, polymer conjugates 9026-93-1DP, Adenosine deaminase, polymer conjugates 9027-69-4DP, Adenosine diphosphatase, polymer conjugates 9027-98-9DP, polymer conjugates 9033-06-1DP, Glucosidase, polymer conjugates 9034-40-6DP, LHRH, polymer conjugates 9054-89-1DP, Superoxide dismutase, polymer conjugates 25104-18-1DP, Poly(L-lysine), conjugates with peptides or proteins 25322-68-3DP, **Polyethylene glycol**, conjugates with peptides or proteins 25322-69-4DP, **Polypropylene glycol**, conjugates with peptides or proteins 26023-30-3DP, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)], conjugates with peptides or proteins 26100-51-6DP, Polylactic acid, conjugates with peptides or proteins 31714-45-1DP, conjugates with peptides or proteins 38000-06-5DP, Poly(L-lysine), conjugates with peptides or proteins 62229-50-9DP, EGF, conjugates with **PEG** derivative 62229-50-9DP, Epidermal growth factor, polymer conjugates 63340-72-7DP, Thymic humoral factor, polymer conjugates 83652-28-2DP, Calcitonin gene related peptide, polymer conjugates 83869-56-1DP, Granulocyte-macrophage colony-stimulating factor, polymer conjugates 113189-02-9DP, Factor VIII, polymer conjugates 143011-72-7DP, Granulocyte colony-stimulating factor, polymer conjugates **395645-02-0DP**, conjugates with peptides or proteins 395645-03-1DP, conjugates with peptides or proteins (highly reactive branched polymers and their conjugates with proteins or peptides)

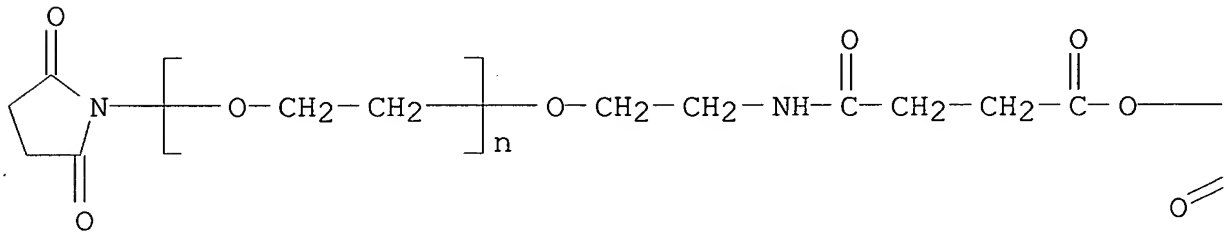
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 40 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 134:331704 HCA
TITLE: Sensitive measurement of polyethylene glycol-modified proteins
AUTHOR(S): Tsai, Nu-Man; Cheng, Tian-Lu; Roffler, Steve R.
CORPORATE SOURCE: Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan
SOURCE: BioTechniques (2001), 30(2), 396-402
CODEN: BTNQDO; ISSN: 0736-6205
PUBLISHER: Eaton Publishing Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

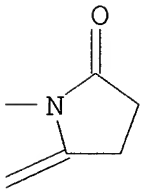
AB An IgM monoclonal antibody (AGP3) against polyethylene glycol (PEG) was used to assay PEG-modified proteins by ELISA. PEG-modified β-glucuronidase could be measured at concns. as low as 15 ng/mL, corresponding to 750 pg (1.8 fmol) of conjugate. This ELISA should be generally applicable to all PEG-modified proteins because AGP3 binds the backbone of the PEG chain independent of the linker used for PEG attachment.

IT **337376-17-7DP**, reaction products with β-glucuronidase
(sensitive measurement of **PEG**-modified proteins)
RN 337376-17-7 HCA
CN Poly(oxy-1,2-ethanediyl), α-(2,5-dioxo-1-pyrrolidinyl)-ω-[2-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]amino]ethoxy]-(9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



CC 64-2 (Pharmaceutical Analysis)
Section cross-reference(s): 9
IT 9001-45-0DP, β-Glucuronidase, reaction products with methoxypolyethylene glycol succinimidylpropionate 174569-25-6DP, reaction products with β-glucuronidase **337376-17-7DP**, reaction products with β-glucuronidase
(sensitive measurement of **PEG**-modified proteins)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 41 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 134:285533 HCA
TITLE: Drug Delivery Systems Employing 1,6-Elimination: Releasable Poly(ethylene glycol) Conjugates of Proteins
AUTHOR(S): Lee, Stanford; Greenwald, Richard B.; McGuire, Jeffrey; Yang, Karen; Shi, Celine
CORPORATE SOURCE: Enzon Inc., Piscataway, NJ, 08854, USA

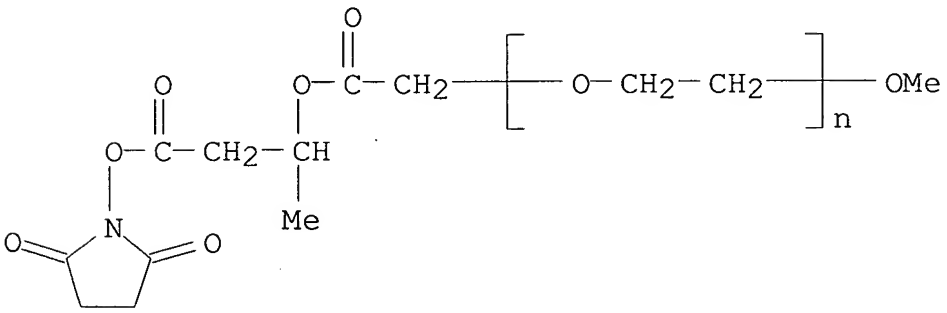
SOURCE: Bioconjugate Chemistry (2001), 12(2), 163-169
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using lysozyme as a representative protein substrate that loses its activity when PEGylation takes place on the ε-amino group of lysine residues, various amts. of a novel releasable PEG linker (rPEG) were conjugated to the protein. RPEG-lysozyme conjugates were relatively stable in pH 7.4 buffer for over 24 h. However, regeneration of native protein from the rPEG conjugates occurred in a predictable manner during incubation in high pH buffer or rat plasma, as demonstrated by enzymic activity and structural characterization. The rates of regeneration were also correlated with PEG number: native lysozyme was released more rapidly from the monosubstituted conjugate than from the disubstituted conjugate, suggesting possible steric hindrance to the approach of cleaving enzymes. Recovery of normal activity and structure for the regenerated native lysozyme was shown by a variety of assays.

IT **214746-64-2P**
(releasable **PEG** conjugates of proteins as drug delivery systems employing 1,6-elimination:)

RN 214746-64-2 HCA

CN Poly(oxy-1,2-ethanediyl), α-[2-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1-methyl-3-oxopropoxy]-2-oxoethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 63-5 (Pharmaceuticals)

IT 4397-14-2P, 3,5-Dimethyl-4-hydroxybenzyl alcohol
214746-64-2P 333794-38-0P 333794-39-1P
(releasable **PEG** conjugates of proteins as drug delivery systems employing 1,6-elimination:)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 42 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 134:266736 HCA
TITLE: Soluble, degradable poly(ethylene glycol) derivatives for controllable release of bound molecules into solution
INVENTOR(S): Harris, J. Milton
PATENT ASSIGNEE(S): Shearwater Corporation, USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6214966	B1	20010410	US 1997-937846	19970925
US 2001021763	A1	20010913	US 2001-824297	20010402
US 6515100	B2	20030204		
US 2003220447	A1	20031127	US 2002-318322	20021212

PRIORITY APPLN. INFO.:			US 1996-26716P	P 19960926
			US 1997-937846	A3 19970925
			US 2001-824297	A1 20010402

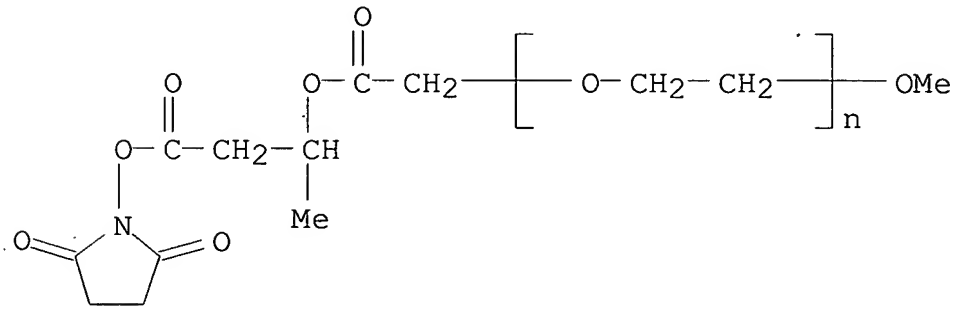
AB PEG and related polymer derivs. having weak, hydrolytically unstable linkages near the reactive end of the polymer are provided for conjugation to drugs, including proteins, enzymes, small mols., and others. These derivs. provide a sufficient circulation period for a drug-PEG conjugate and then for hydrolytic breakdown of the conjugate and release of the bound mol. In some cases, drugs that previously had reduced activity when permanently coupled to PEG can have therapeutically suitable activity when coupled to a degradable PEG in accordance with the invention. The PEG of the invention can be used to impart water solubility, size, slow rate of kidney clearance,

and reduced immunogenicity to the conjugate. Controlled hydrolytic release of the bound mol. in the aqueous environment can then enhance the drug delivery system. Polyethylene glycol Me 2-(2-pyridyldithio)ethoxycarbonylmethyl ether was prepared and the hydrolytic half-life of the ester linkage determined

IT **214746-64-2P**
(soluble, degradable **polyethylene glycol** derivs. for controllable release of bound mols. into solution)

RN 214746-64-2 HCA

CN Poly(oxy-1,2-ethanediyl), α-[2-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1-methyl-3-oxopropoxy]-2-oxoethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM A61K031-765
ICS A61K031-785; C08G073-10; C08G063-48

NCL 528322000

CC 35-8 (Chemistry of Synthetic High Polymers)
Section cross-reference(s): 63

IT 214042-74-7P 214042-78-1P **214746-64-2P** 331968-53-7P
331968-54-8P 331968-57-1P 331968-58-2P 331968-60-6P
331968-61-7P **331968-63-9P** 331968-64-0P 331968-65-1P
331968-66-2P 331968-68-4P 331968-70-8P 331968-72-0P
331968-74-2P 331968-75-3P 331968-77-5P
(soluble, degradable **polyethylene glycol** derivs. for controllable release of bound mols. into solution)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 43 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 134:204694 HCA
TITLE: New PEGs for peptide and protein modification, suitable for identification of the PEGylation site
AUTHOR(S): Veronese, F. M.; Sacca, B.; de Laureto, P. Polverino; Sergi, M.; Caliceti, P.; Schiavon, O.; Orsolini, P.

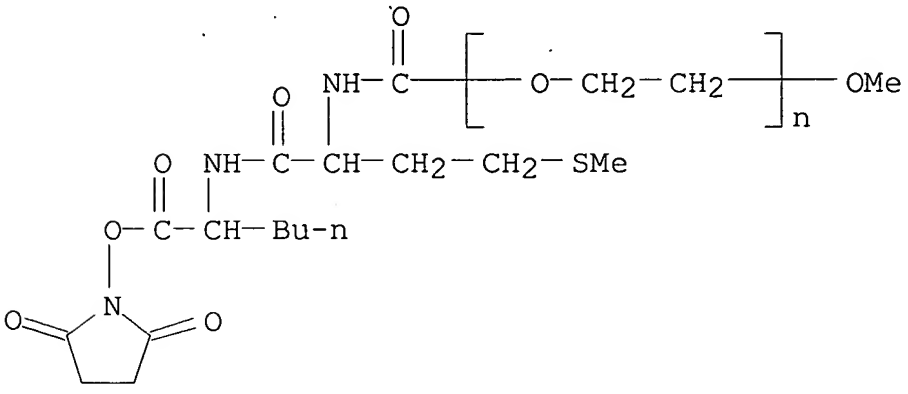
CORPORATE SOURCE: Department of Pharmaceutical Sciences (CNR Center for Chemical Investigation of Drugs), University of Padova, Padua, 35131, Italy
SOURCE: Bioconjugate Chemistry (2001), 12(1), 62-70
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB New PEG derivs. were studied for peptide and protein modification, based upon an amino acid arm, Met-Nle or Met-βAla, activated as succinimidyl ester. PEG-Met-Nle-OSu or PEG-Met-βAla-OSu react with amino groups in protein-yielding conjugates with stable amide bond. From these conjugates PEG may be removed by BrCN treatment, leaving Nle or βAla as reporter amino acid, at the site where PEG was bound. The conjugation of PEG and its removal by BrCN treatment was assessed on a partial sequence of glucagone and on lysozyme as model peptide or protein. Furthermore, insulin, a protein with three potential sites of PEGylation, was modified by PEG-Met-Nle, and the PEG isomers were separated by HPLC. After removal of PEG, as reported above, the sites of PEGylation were identified by characterization of the two insulin chains obtained after reduction and carboxymethylation. Mass spectrometry, amino acid anal. and Edman sequence, could reveal the position of the reporter norleucine that corresponds to the position of PEG binding.

IT **329024-01-3DP**, reaction products with peptides and proteins (**PEGs** for peptide and protein modification for identification of PEGylation site)

RN 329024-01-3 HCA

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-methoxy-, ester with 1-[(N-carboxy-L-methionyl-L-norleucyl)oxy]-2,5-pyrrolidinedione (9CI) (CA INDEX NAME)



CC 9-16 (Biochemical Methods)

Section cross-reference(s): 63
IT 9001-63-2DP, Lysozyme, reaction products with PEG peptide
9004-10-8DP, Insulin, reaction products with PEG peptide, preparation **329024-01-3DP**, reaction products with peptides and proteins
(**PEGs** for peptide and protein modification for identification of PEGylation site)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 44 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 134:183490 HCA
TITLE: Hydrophilic and lipophilic balanced microemulsion formulations of free-form and/or conjugation-stabilized therapeutic agents such as insulin
INVENTOR(S): Ekwuribe, Nnochiri Nkem; Ramaswamy, Muthukumar; Radhakrishnan, Balasingam; Allaudeen, Hameedsulthan S.
PATENT ASSIGNEE(S): Protein Delivery, Inc., USA
SOURCE: U.S., 32 pp., Cont.-in-part of U. S. 5,681,811. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6191105	B1	20010220	US 1997-958383	19971027
US 5359030	A	19941025	US 1993-59701	19930510
US 5438040	A	19950801	US 1994-276890	19940719
US 5681811	A	19971028	US 1995-509422	19950731
US 2003229006	A1	20031211	US 2003-448524	20030530
US 2003229010	A1	20031211	US 2003-448535	200306

PRIORITY APPLN. INFO.:

US 1993-59701	A3	02 199305 10
US 1994-276890	A2	 199407 19
US 1995-509422	A2	 199507 31
US 1997-958383	A3	 199710 27
US 2000-614203	A1	 200007 12

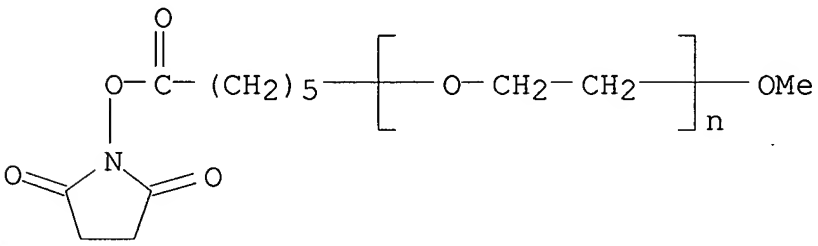
AB A therapeutic formulation comprising a microemulsion of a therapeutic agent in free and/or conjugate coupled form, wherein the microemulsion comprises a water-in-oil (w/o) microemulsion including a lipophilic phase and a hydrophilic phase, and has a hydrophilic and lipophilic balance (HLB) value between 3 and 7 is described. The therapeutic agent is selected from the group consisting of insulin, calcitonin, ACTH, glucagon, somatostatin, somatotropin, somatomedin, parathyroid hormone, erythropoietin, hypothalamic releasing factors, prolactin, thyroid stimulating hormones, endorphins, enkephalins, vasopressin, non-naturally occurring opioids, superoxide dismutase, interferon, asparaginase, arginase, arginine deaminease, adenosine deaminase, RNase, trypsin, chymotrypsin, papain, Ara-A (Arabinofuranosyladenine), acylguanosine, nordeoxyguanosine, azidothymidine, dideoxyadenosine, dideoxycytidine, dideoxyinosine, floxuridine, 6-mercaptopurine, doxorubicin, daunorubicin, or I-darubicin, erythromycin, vancomycin, oleandomycin, ampicillin, quinidine and heparin. In a particular aspect, the invention comprises an insulin composition suitable for parenteral as well as non-parenteral administration, preferably oral or parenteral administration, comprising insulin covalently coupled with a polymer including (i) a linear **polyalkylene glycol** moiety and (ii) a lipophilic moiety, wherein the insulin, the linear **polyalkylene glycol** moiety and the lipophilic moiety are conformationally arranged in relation to one another such that the insulin in the composition has an enhanced in vivo resistance to enzymic degradation, relative to insulin alone.

The microemulsion compns. of the invention are usefully employed in therapeutic as well as non-therapeutic, e.g., diagnostic, applications. For example, a microemulsion formulation was prepared containing Capmul MCM 53.0, Centrophase 31 5.7, propylene glycol 19.9, Tween 80 1.4, hexyl insulin in NaP buffer 15 mg/mL, and NaP buffer up to 100%, resp. Also, preparation of hexyl insulin conjugates with Me (ethylene glycol)7-O-hexanoic acid was carried out.

IT **212969-35-2P**
(hydrophilic and lipophilic balanced microemulsions of free and/or conjugated drugs such as insulin)

RN 212969-35-2 HCA

CN Poly(oxy-1,2-ethanediyl), α-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM A61K038-38
ICS C07K014-62

NCL 514003000

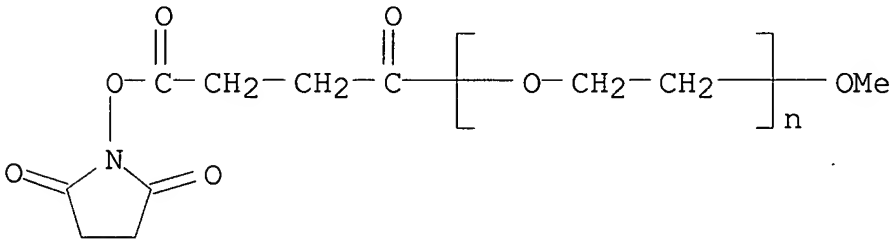
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2

IT 7075-11-8DP, tri-Bu derivative 88517-92-4P 100601-63-6P 161756-38-3P 161756-39-4P **212969-35-2P** 326892-08-4P 326892-09-5P
(hydrophilic and lipophilic balanced microemulsions of free and/or conjugated drugs such as insulin)

IT 9004-95-9DP, Polyoxyethylene cetyl ether, conjugates with tri-Bu AraCMP 9004-99-3DP, Polyethylene glycol monostearate, conjugates with insulin 9005-66-7DP, conjugates with insulin 9005-70-3DP, conjugates with polysorbate trioleate 11070-73-8DP, Bovine insulin, conjugates 25322-68-3DP, Polyethylene glycol, conjugates with tetrahydropyran derivative and insulin 88517-92-4DP, conjugates with insulin and polyethylene glycol **212969-35-2DP**, conjugates with hexyl insulin
(hydrophilic and lipophilic balanced microemulsions of free and/or conjugated drugs such as insulin)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 45 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 133:331421 HCA
TITLE: Chemical modification of Escherichia coli L-asparaginase with polyethylene glycol
AUTHOR(S): Zhou, Xiao-Yan; Liu, Jing-Jing
CORPORATE SOURCE: Departement of Biochemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Zhongguo Yaoke Daxue Xuebao (2000), 31(3), 230-233
CODEN: ZHYXE9; ISSN: 1000-5048
PUBLISHER: Zhongguo Yaoke Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB E. coli L-asparaginase was modified with SS-PEG [methoxypolyethylene glycolyl succinimidyl succinate] which was prepared in two steps. The modified enzyme activity was maintained 44. 52% while the antigenicity was greatly reduced. The modified L-asparaginase showed greater resistance to trypsin degradation
IT **78274-32-5DP**, reaction products with L-asparaginase
(chemical modification of Escherichia coli L-asparaginase with **polyethylene glycol**)
RN 78274-32-5 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 7-8 (Enzymes)
IT **78274-32-5DP**, reaction products with L-asparaginase
(chemical modification of Escherichia coli L-asparaginase with **polyethylene glycol**)

L24 ANSWER 46 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 133:125062 HCA
TITLE: B-Domain Deleted Recombinant Coagulation Factor VIII Modified with Monomethoxy Polyethylene Glycol
AUTHOR(S): Roestin, Johanna; Smeds, Anna-Lisa; Aakerblom, Eva
CORPORATE SOURCE: Recombinant Factor VIII R&D, Pharmacia & Upjohn,

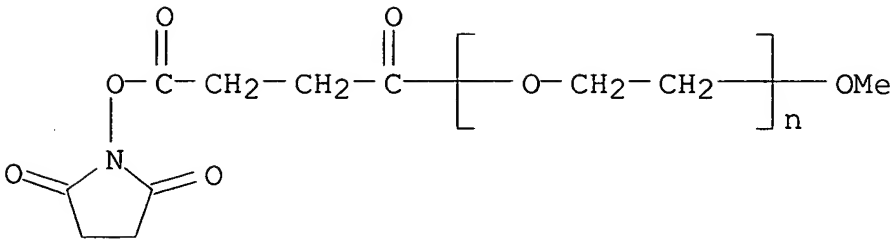
Stockholm, S-112 87, Swed.
SOURCE: Bioconjugate Chemistry (2000), 11(3), 387-396
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recombinant coagulation factor VIII (r-VIII SQ) was chemical modified with monomethoxy poly(ethylene glycol) (mPEG). Three mPEG derivs. were used for coupling to the r-VIII SQ lysines, a mixed anhydride of monomethoxy poly(ethylene glycol) succinic acid (mPEG-SAH), monomethoxy poly(ethylene glycol) succinimidyl succinate (mPEG-SS), and monomethoxy poly(ethylene glycol) tresylate (mPEG-TRES). A consequence of the modification with all derivs. was a substantial reduction in coagulant activity, even at very low degrees of modification. A method was developed with the purpose of avoiding conjugation at certain important biol. sites on the factor VIII and thereby producing conjugates with better retained activity. This was achieved by immobilizing the protein onto a solid matrix during the modification reaction. Characterization of conjugates by SDS-PAGE, western blots, interaction with von Willebrand factor (vWf), and thrombin activation/inactivation analyses was undertaken. The SDS-PAGE and western blots revealed coupling heterogeneity regarding degree of modification. The amount of factor VIII able to bind to vWf decreased with the conjugation. Thrombin activated the modified factor VIII to essentially the same extent as the reference preparation of r-VIII SQ. Inactivation of the modified factor VIII was, however, slower than inactivation of the unmodified protein. Finally, an in vitro study was performed to evaluate the influence of the mPEG modification on the protein stability in extract of porcine tissue. Despite that conjugates with low degrees of modification were included in the study, the coagulant activity was preserved to a significantly higher extent in all incubation mixts. containing conjugates compared to that with unmodified protein.

IT **78274-32-5DP**, reaction products with Factor VIII (B-domain deleted recombinant coagulation Factor VIII modified with monomethoxy **PEG**)

RN 78274-32-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 63-5 (Pharmaceuticals)
IT 9001-27-8DP, Factor VIII, reaction products with PEG derivs.
31961-02-1DP, reaction products with Factor VIII
78274-32-5DP, reaction products with Factor VIII
121559-53-3DP, reaction products with Factor VIII
(B-domain deleted recombinant coagulation Factor VIII modified with monomethoxy **PEG**)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

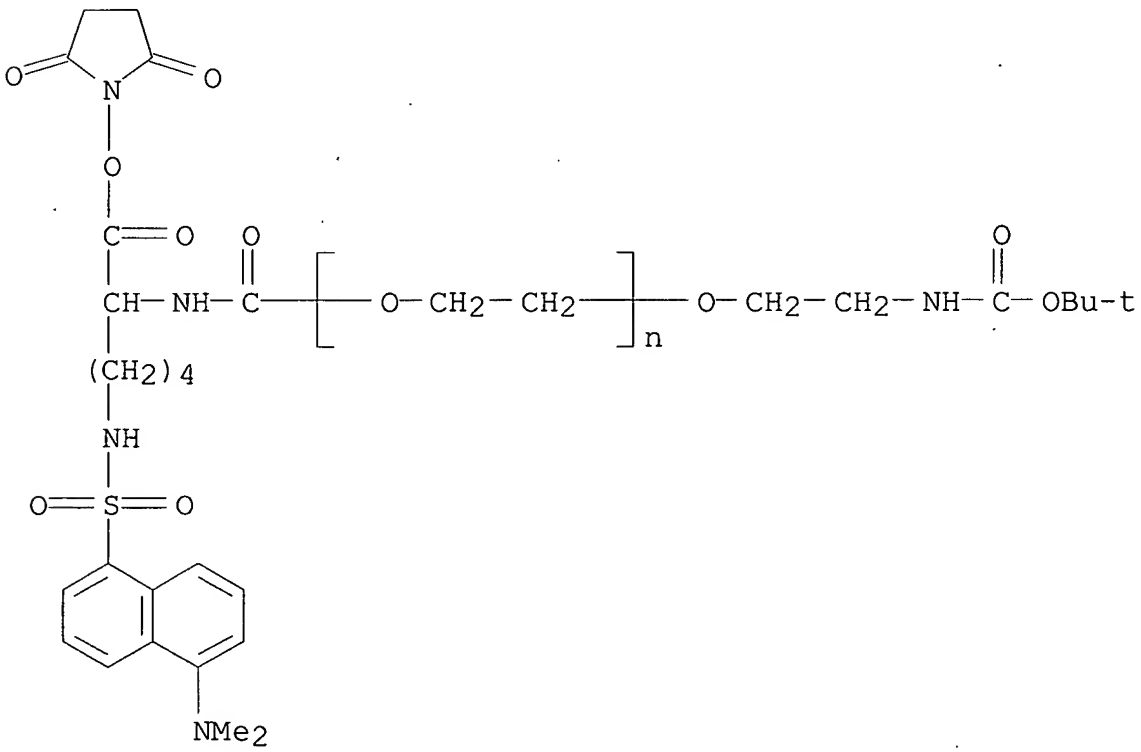
L24 ANSWER 47 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 133:94381 HCA
TITLE: Fluorescent-Labeled Poly(ethylene glycol) Lipid Conjugates With Distal Cationic Headgroups
AUTHOR(S): Chen, Tao; Wong, Kim F.; Fenske, David B.; Palmer, Lorne R.; Cullis, Pieter R.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, BC, V6T 1Z3, Can.
SOURCE: Bioconjugate Chemistry (2000), 11(3), 433-437
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis of a new class of fluorescent cationic poly(ethylene glycol) lipid conjugates (CPLs) is described. These lipids consist of a hydrophobic distearoyl-phosphatidylethanolamine (DSPE) anchor coupled to a highly fluorescent Nε-dansyl lysine moiety, which is attached to a hydrophilic PEG spacer that is linked to a cationic headgroup made of lysine residues. Introduction of the dansyl moiety allows rapid and accurate quantification of CPLs within lipid bilayers using fluorescence techniques. The synthetic scheme is straightforward, using repeated amino-carboxyl coupling reaction steps, with purification by precipitation A series of dansylated CPLs
was synthesized with zero, one, three, and seven lysine residues located at the distal end of the PEG chain, giving rise to CPLs with

one, two, four, and eight distal pos. charges, resp. The structures of the CPLs were confirmed by 1H NMR spectroscopy and chemical anal. CPLs provide a means of introducing pos. charge to a bilayer that is localized some distance from the membrane surface, and are of particular interest for nonviral gene delivery applications. The usefulness of CPLs is demonstrated by the enhanced in vitro cellular binding and uptake of liposomes containing CPL4.

IT **280577-49-3P**
(fluorescent-labeled **PEG** lipid conjugates With distal cationic headgroups)

RN 280577-49-3 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[(1S)-5-[[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]amino]-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]pentyl]amino]carbonyl]-ω-[2-[[(1,1-dimethylethoxy)carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)



CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 34, 35

IT 280577-48-2P **280577-49-3P** 280577-50-6P 280577-52-8P 280577-54-0P 280577-56-2P
(fluorescent-labeled **PEG** lipid conjugates With distal cationic headgroups)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE

IN THE RE FORMAT

L24 ANSWER 48 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 132:298578 HCA
TITLE: Synthesis and characterization of a poly-L-lysine-polyethylene glycol-lactose delivery vehicle for gene delivery
AUTHOR(S): Lentz, M. J.; Kim, S. W.
CORPORATE SOURCE: Center of Controlled Chemical Delivery, Department of Pharmaceutics and Pharmaceutical Chemistry, University of Utah, Salt Lake City, UT, 84112, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1999), 26th, 809-810
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

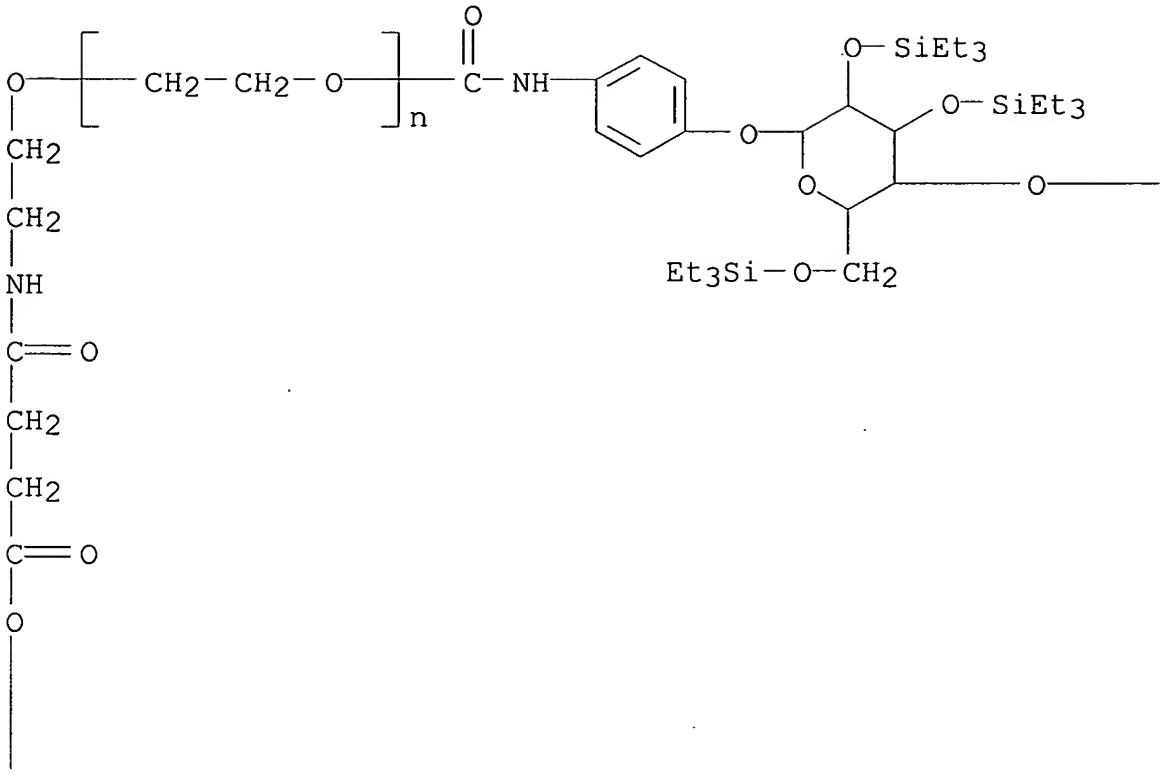
AB FMOC-PEG-NHS (MW 3400) was conjugated to p-aminophenyl β-D-lactopyranoside. The hydroxyl groups on the lactose are blocked with triethylsilyl protecting groups. The FMOC (amino protecting group) is removed with piperidine in DMF and the amine is converted into a carboxylic acid via reaction with succinic anhydride. The carboxylic acid is converted into a NHS ester using N,N'-dicyclohexylcarbodiimide and N-hydroxysuccinimide. The NHS ester is then reacted with the ε-amine of poly-L-lysine (20K-28K MW) giving a comb-shaped polymer where the PEG-lactose groups are grafted off of the lysine groups. Finally, the hydroxyl protecting groups are removed using tetrabutylammonium fluoride. A 50% yield was obtained between the linkage of FMOC-PEG-NHS and amino-phenyl-lactopyranoside. As polyamine carriers become more sophisticated, it is important to make sure that what is chemical synthesized is correct.

IT **264257-56-9DP**, reaction products with poly-L-lysine (synthesis and characterization of a poly-L-lysine-**polyethylene glycol**-lactose delivery vehicle for gene delivery)

RN 264257-56-9 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[4-[[4-O-[2,3,4,6-tetrakis-O-(triethylsilyl)-β-D-galactopyranosyl]-2,3,6-tris-O-(triethylsilyl)-α-D-glucopyranosyl]oxy]phenyl]amino]carbonyl]-ω-[2-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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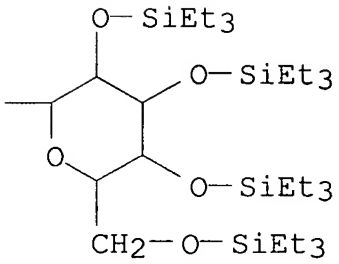

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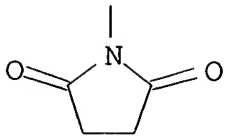
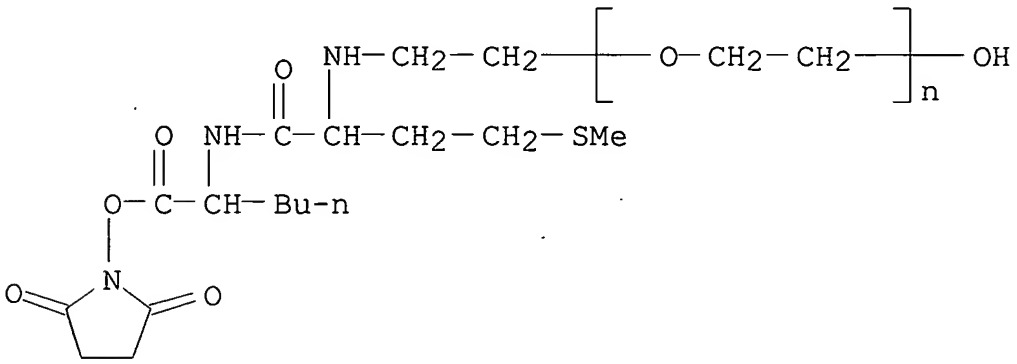


CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3
IT 25104-18-1DP, Poly-L-lysine, reaction products with PEG-aminophenyllactopyranoside 38000-06-5DP, Poly-L-lysine, reaction products with PEG-aminophenyllactopyranoside **264257-56-9DP**, reaction products with poly-L-lysine
(synthesis and characterization of a poly-L-lysine-**polyethylene glycol**-lactose delivery vehicle for gene delivery)
IT **264257-56-9P** 264257-57-0P 264257-58-1P 264257-59-2P 264257-60-5P
(synthesis and characterization of a poly-L-lysine-**polyethylene glycol**-lactose delivery vehicle for gene delivery)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 49 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 132:269917 HCA
TITLE: PEG peptide and protein drug delivery: a procedure to identify the pegylation site
AUTHOR(S): Veronese, F. M.; Sacca, B.; Schiavon, O.; Caliceti, P.; Orsatti, L.; Orsolini, P.
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of Padova, Padua, 35100, Italy
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1999), 26th, 106-107
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PEG-Met-Nle-OSu was prepared so that on selective removal of the PEG chain the unnatural amino acid norleucine is left which is a suitable reporter group attached to a protein where PEG was linked. This approach was demonstrated showing the possibility of removing PEG in mild conditions from lysozyme and insulin and to identify the site of conjugation by classical procedures of peptide sequence in the case of insulin.

IT **263368-89-4P**
(a procedure to identify the pegylation site in **PEG** peptide and protein drug delivery)
RN 263368-89-4 HCA
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, monoether with 1-[[N-(2-hydroxyethyl)-L-methionyl-L-norleucyl]oxy]-2,5-pyrrolidinedione (9CI) (CA INDEX NAME)



CC 63-5 (Pharmaceuticals)
IT **263368-89-4P**
(a procedure to identify the pegylation site in **PEG** peptide and protein drug delivery)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 50 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 131:291115 HCA
TITLE: A genetically modified recombinant tumor necrosis factor-α conjugated to the distal terminals of liposomal surface grafted polyethylene glycol chains
AUTHOR(S): Savva, Michalakis; Duda, Erno; Huang, Leaf
CORPORATE SOURCE: Departments of Pharmaceutical Sciences and Pharmacology, University of Pittsburgh, Pittsburgh, PA, USA
SOURCE: International Journal of Pharmaceutics (1999), 184(1), 45-51
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A genetically modified recombinant tumor necrosis factor (TNF)-α (rKRKTNF) was conjugated to the terminal carboxyl groups of liposome grafted PEG chains. The long-circulating

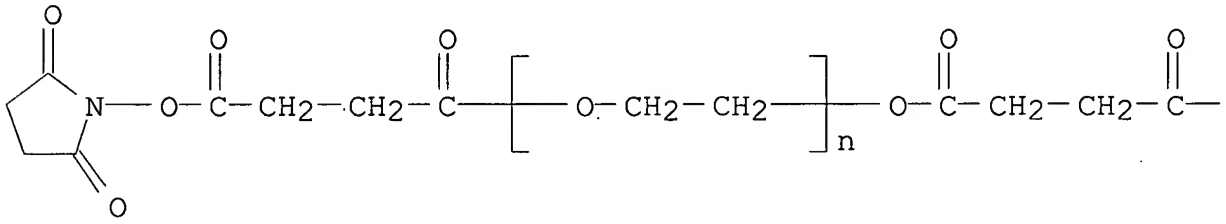
liposomes were composed of egg phosphatidylcholine, cholesterol (chol) and 7% carboxyl PEG-phosphatidylethanolamine. The conjugation efficiency of the genetically modified rKRKTNF under the conditions described in the text was approx. 55%. The biol. activity of liposomal rKRKTNF, as tested with an in vitro cytotoxicity assay was reduced compared to the free, unconjugated rKRKTNF. In vivo biodistribution studies showed that conjugation of as little as 0.13% of the grafted PEG chains resulted in a rapid elimination of the formulation from the blood stream. It is speculated that both non-selective conjugate chemical and inherent recognition of the TNF by the components of the reticuloendothelial system (RES) are responsible for the short blood half life of the rKRKTNF-PEG-liposomes. The result suggest that conjugating a rapidly clearing recombinant cytokine to long-circulating liposomes provides little advantage in modifying the pharmacokinetic parameters of the cytokine.

IT **85419-94-9P**
(a genetically modified recombinant tumor necrosis factor-α conjugated to distal terminals of liposomal surface grafted **PEG** chains)

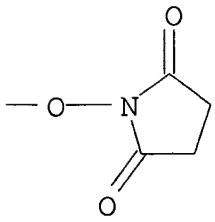
RN 85419-94-9 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



CC 63-5 (Pharmaceuticals)

IT **85419-94-9P** 246024-61-3P
(a genetically modified recombinant tumor necrosis factor-α conjugated to distal terminals of liposomal surface grafted **PEG** chains)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 51 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 131:219155 HCA
TITLE: Polyethylene glycol derivatives with proximal reactive groups
INVENTOR(S): Harris, J. Milton; Kozlowski, Antoni
PATENT ASSIGNEE(S): Shearwater Polymers, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945964	A1	19990916	WO 1999-US5333	19990311
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2323048	AA	19990916	CA 1999-2323048	19990311
AU 9929038	A1	19990927	AU 1999-29038	19990311
EP 1061954	A1	20001227	EP 1999-909959	19990311
EP 1061954	B1	20040609		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

US 2001011115	A1	20010802	US 1999-265989	199903 11
US 6362254	B2	20020326		
JP 2002506087	T2	20020226	JP 2000-535377	199903 11
EP 1411075	A2	20040421	EP 2003-28370	199903 11
EP 1411075	A3	20040728		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 268609	E	20040615	AT 1999-909959	199903 11
US 2002037949	A1	20020328	US 2001-992129	200111 05
US 6437025	B2	20020820		
US 2002040076	A1	20020404	US 2001-992102	200111 05
US 6664331	B2	20031216		
US 2002052430	A1	20020502	US 2001-993088	200111 05
US 6541543	B2	20030401		
US 2004059025	A1	20040325	US 2003-668456	200309 23
PRIORITY APPLN. INFO.:			US 1998-77700P A1	199803 12
			EP 1999-909959 A3	199903 11
			US 1999-265989 A3	199903 11
			WO 1999-US5333 W	199903 11
			US 2001-992102 A1	

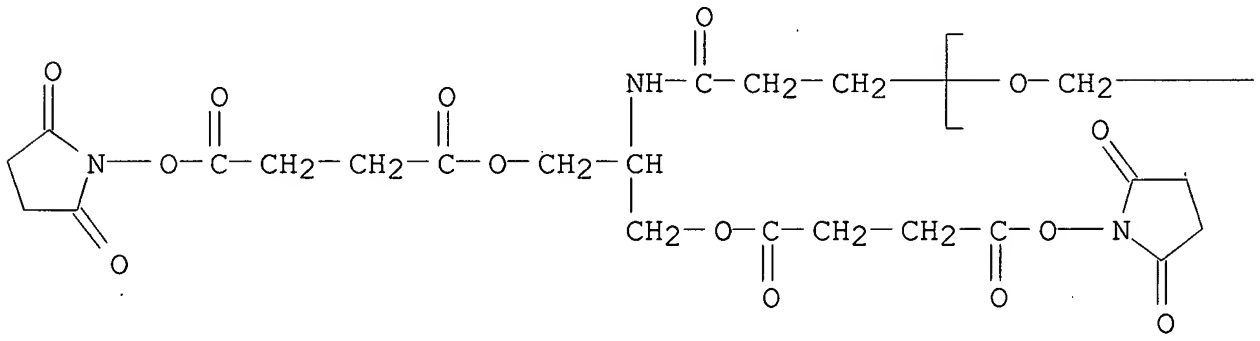
AB An activated, substantially water-soluble polyethylene glycol (PEG) is provided having a linear or branched PEG backbone and at least one terminus linked to the backbone through a hydrolytically stable linkage, wherein the terminus is branched and has proximal reactive groups. The free reactive groups are capable of reacting with active moieties in a biol. active agent such as a protein or peptide thus forming conjugates between the activated PEG and the biol. active agent. One example given is the preparation of methoxy-PEG20K-OCH2CH2CONHCH(CH2O2CCH2CH2CONS)2.

IT **243468-56-6P**
(**polyethylene glycol** derivs. with proximal reactive groups for coupling to bioactive compds.)

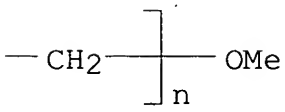
RN 243468-56-6 HCA

CN Poly(oxy-1,2-ethanediyl), α-[3-[[2-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]-1-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]methyl]ethyl]amino]-3-oxopropyl]-ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



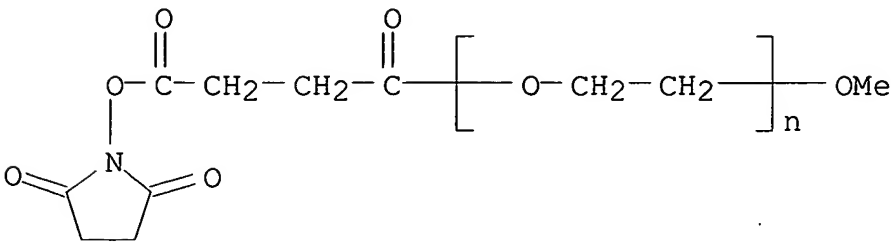
IC ICM A61K047-48
ICS C08G065-32

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 35
IT **243468-56-6P** 243468-64-6P **243468-67-9P**
243468-68-0P
(**polyethylene glycol** derivs. with proximal reactive groups for coupling to bioactive compds.)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 52 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 131:161509 HCA
TITLE: Activity of amphipathic polyethylene glycols to prolong the circulation time of liposomes
AUTHOR(S): Yuda, Tsutomu; Pongpaibul, Yanee; Maruyama, Kazuo; Iwatsuru, Motoharu
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Teikyo University, Kanagawa, 199-0195, Japan
SOURCE: Yakuzaigaku (1999), 59(1), 32-42
CODEN: YAKUA2; ISSN: 0372-7629
PUBLISHER: Nippon Yakuzai Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have studied the reticuloendothelial-avoidance mechanisms of PEG liposomes in vivo and in vitro. Only relatively small liposomes (diameter < 200 nm) had their circulation time prolonged by the inclusion of amphipathic PEG. Increasing the size of PEG liposomes led to significant spleen uptake, probably via a filter mechanism. However, a study of the biodistribution in splenectomized mice showed that large-sized PEG liposomes have an intrinsic ability for long circulation in vivo. The presence of PEG reduced the distribution of liposomes into nonparenchymal cells in the liver. These results are consistent with the significantly reduced uptake of PEG liposomes by J774 cells, a murine macrophage-like cell line. The proteins associated with liposomes in vivo were analyzed by SDS-polyacrylamide gel electrophoresis and immunoblot anal. after isolation by using a spin column procedure. Data showed that PEG on the surface of liposome prevents the binding of complement 3 (C3) to the liposome. An in vitro experiment using an avidin-biotin agglutination assay of liposomes also showed that the PEG chains sterically block avidin-biotin binding. These studies suggested that PEG prolongs liposome circulation time by providing a strong steric barrier which prevents close contact with serum protein (complement) and RES cells (macrophages).
IT **78274-32-5P**
(activity of amphipathic **polyethylene glycols** to prolong the circulation time of liposomes)
RN 78274-32-5 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-

1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 63-5 (Pharmaceuticals)
IT **78274-32-5P**
(activity of amphipathic **polyethylene glycols** to prolong the circulation time of liposomes)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 53 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 131:106800 HCA
TITLE: Degradable heterobifunctional polyethylene glycol acrylates and gels and conjugates
INVENTOR(S): Harris, J. Milton; Zhao, Xuan
PATENT ASSIGNEE(S): Shearwater Polymers, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9934833	A1	19990715	WO 1999-US594	19990106
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2316834	AA	19990715	CA 1999-2316834	

				19990106
AU 9922214	A1	19990726	AU 1999-22214	19990106
AU 755051	B2	20021205		
EP 1053019	A1	20001122	EP 1999-902172	19990106
EP 1053019	B1	20031203		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6362276	B1	20020326	US 1999-226341	19990106
JP 2003510375	T2	20030318	JP 2000-527280	19990106
AT 255422	E	20031215	AT 1999-902172	19990106
PT 1053019	T	20040430	PT 1999-902172	19990106
ES 2211033	T3	20040701	ES 1999-902172	19990106
US 2001016624	A1	20010823	US 2001-824395	20010402
US 2004086991	A1	20040506	US 2003-684692	20031014
US 2004086992	A1	20040506	US 2003-684946	20031014
PRIORITY APPLN. INFO.:			US 1998-70680P P	19980107
			US 1999-226341 A3	19990106
			WO 1999-US594 W	19990106

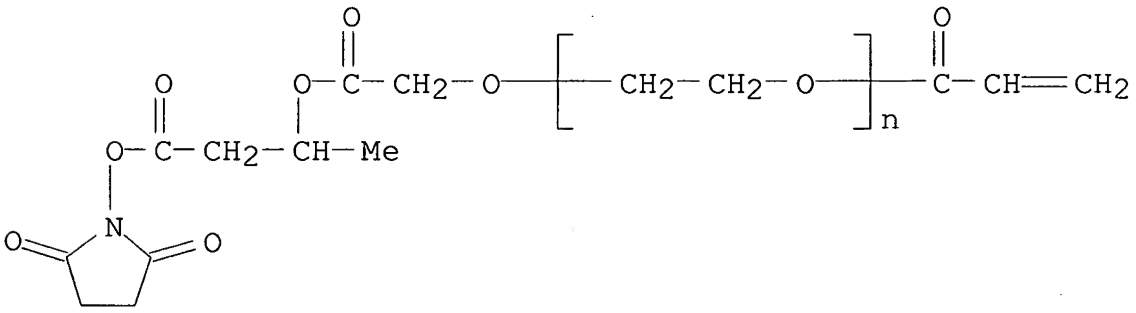
US 2001-824395 B1
200104
02

AB A heterobifunctional poly(ethylene glycol) is provided having a hydrolytically degradable linkage, a first terminus comprising an acrylate group, and a second terminus comprising a target such as a protein or pharmaceutical agent or a reactive moiety capable of coupling to a target. Hydrogels are prepd and can be used as carriers for a protein or a pharmaceutical that can be readily released in a controlled fashion. CH2:CHCO2-PEG-OCH2OCH2CO2CHMeCH2CO2-NS (I) (where NS = N-hydroxuccinimidyl) was prepared by the conversion of BzO-PEG-OCH2CO2H to the acid chloride, treatment of the resulting acid chloride with 3-hydroxybutyric acid,,hydrogenolysis, reaction with acryloyl chloride followed by treatment with N-hydroxysuccinimide. I was then treated with lucifer-yellow modified lysozyme solution and the solution was stored at
4° prior to release studies.

IT **230614-82-1P**
(**preparation** of degradable heterobifunctional **PEG** acrylates and gels and conjugates)

RN 230614-82-1 HCA

CN Poly(oxy-1,2-ethanediyl), α-(1-oxo-2-propenyl)-ω-[2-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1-methyl-3-oxopropoxy]-2-oxoethoxy]- (9CI) (CA INDEX NAME)



IC A61K047-48

CC 63-6 (Pharmaceuticals)

IT 230614-76-3P 230614-78-5P 230614-79-6P 230614-81-0P
230614-82-1P
(**preparation** of degradable heterobifunctional **PEG** acrylates and gels and conjugates)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 54 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 128:261962 HCA
TITLE: Polyethylene glycol conjugated nanoErythrosomes, method of making same and use thereof
INVENTOR(S): Gaudreault, Rene; Bellemare, Francois
PATENT ASSIGNEE(S): Diagnocure Inc., Can.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811919	A2	19980326	WO 1997-CA698	19970919
WO 9811919	A3	19980604		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2266388	AA	19980326	CA 1997-2266388	19970919
AU 9743732	A1	19980414	AU 1997-43732	19970919
EP 929317	A2	19990721	EP 1997-941755	19970919
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001501190	T2	20010130	JP 1998-514033	19970919

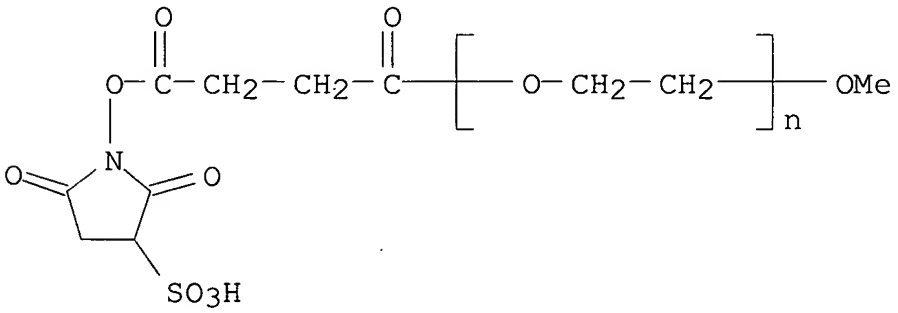
PRIORITY APPLN. INFO.:	US 1996-26363P	P 19960919
	WO 1997-CA698	W 19970919

AB The present invention relates to nanoErythrosomes (Hb-free erythrocyte ghosts), a Drug Delivery System (DDS). More specifically, the present invention relates to a new method of production of nanoErythrosomes. Moreover, the present invention relates to nanoErythrosome compns. having a decreased immunogenic potential and to the use thereof in diagnostic and therapeutic methods. The invention further relates to the bioassays using the nanoErythrosome composition of the present invention to diagnose or prognose a predetd. condition in an animal, as well as kits containing those nanoErythrosomes compns. Methoxy-PEG-S-succinimidyl succinate was conjugated to nanoErythrosomes.

IT **172989-60-5DP**, conjugates with nanoErythrosomes (**PEG** conjugated nanoErythrosomes)

RN 172989-60-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-3-sulfo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM A61K047-48

CC 63-6 (Pharmaceuticals)

IT 71-44-3DP, Spermine, PEG moiety containing, conjugates with nanoErythrosomes 110-60-1DP, Putrescine, PEG moiety containing, conjugates with nanoErythrosomes 124-20-9DP, Spermidine, PEG moiety containing, conjugates with nanoErythrosomes 6539-14-6DP, conjugates with nanoErythrosomes 25322-68-3DP, conjugates with nanoErythrosomes 64987-85-5DP, SMCC, conjugates with nanoErythrosomes **172989-60-5DP**, conjugates with nanoErythrosomes 205368-19-0DP, conjugates with nanoErythrosomes (**PEG** conjugated nanoErythrosomes)

L24 ANSWER 55 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 128:221659 HCA

TITLE: Non-antigenic amine-derived polymers and polymer

conjugates

INVENTOR(S): Greenwald, Richard B.; Martinez, Anthony; Pendri, Annapurna

PATENT ASSIGNEE(S): Enzon, Inc., USA

SOURCE: U.S., 13 pp., Cont.-in-part of U.S. Ser. No. 265,593, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5730990	A	19980324	US 1995-465403	19950605
CA 2191726	AA	19960104	CA 1995-2191726	19950623
US 5902588	A	19990511	US 1997-974532	19971119
US 6177087	B1	20010123	US 1998-184910	19981103

PRIORITY APPLN. INFO.:

US 1994-265593	B2	19940624
US 1995-465403	A3	19950605
US 1997-974532	A3	19971119

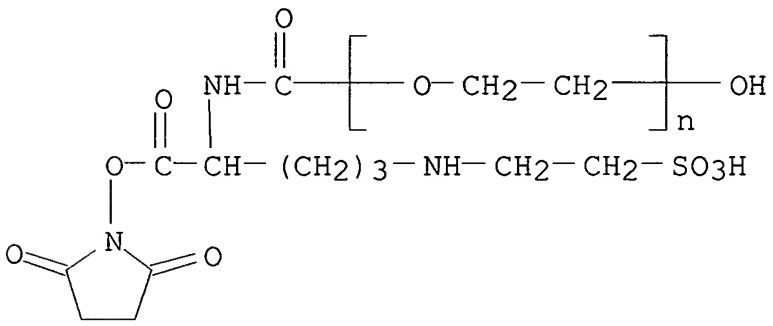
AB Substantially non-antigenic polymers containing pI and/or pH optimum modulating moieties are disclosed. The polyethylene glycol (PEG) derivs. are useful as intermediates for synthesis of amine-based polymers and in the formation of activated polymers for conjugation with nucleophiles. Conjugates and methods of preparation and treatment with the conjugates are also disclosed. Thus, piperazine with a 3-hydroxypropyl group on one N and PEG Me ether on the other was treated with Et 3-isocyanatopropionate and the carbamate product was

hydrolyzed and esterified with N-hydroxysuccinimide, and the ester was then aminolyzed with benzylamine to give a non-antigenic carbamate benzylamide derivative of PEG.

IT **204201-15-0P**
(**preparation** of non-antigenic amine derivs. of **polyethylene glycol**)

RN 204201-15-0 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-4-[(2-sulfoethyl)amino]butyl]amino]carbonyl]-ω-hydroxy-, monosodium salt, (S)- (9CI) (CA INDEX NAME)



● Na

IC ICM A61K045-00
ICS A61K031-74; C08G063-48; C08G063-91

NCL 424279100

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 37

IT 174569-17-6P 174569-20-1DP, reaction products with Hb
174569-24-5P 174569-32-5P **204201-15-0P**
(**preparation** of non-antigenic amine derivs. of **polyethylene glycol**)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 56 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 128:45586 HCA

TITLE: Antibodies directed against dithiocarbamates

INVENTOR(S): Lai, Ching San

PATENT ASSIGNEE(S): Medinox, Inc., USA; Lai, Ching-San

SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

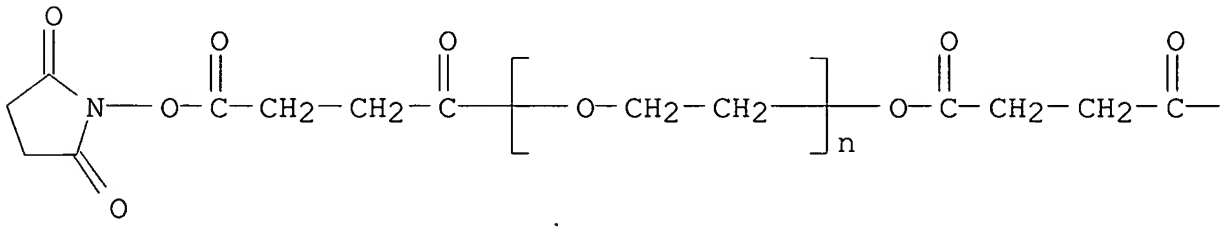
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9743645	A1	19971120	WO 1997-US7380	19970501
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5869348	A	19990209	US 1996-644961	19960515
AU 9727503	A1	19971205	AU 1997-27503	19970501
PRIORITY APPLN. INFO.:			US 1996-644961 A1	19960515
			WO 1997-US7380 W	19970501

OTHER SOURCE(S): MARPAT 128:45586

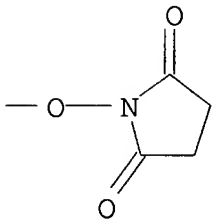
AB In accordance with the present invention, ELISA methods for the measurement of NO levels in mammalian body fluids utilizing monoclonal antibodies directed against dithiocarbamates and related iron complexes are described. It has been found that conjugation of dithiocarbamates to a macromol. produces immunogenic dithiocarbamate-macromol. derivs. Such derivs. can be used for the production (e.g., in rodents) of monoclonal antibodies directed against different forms of dithiocarbamates (e.g., free dithiocarbamates, as well as complexes thereof with iron and, optionally, nitric oxide). In contrast, non-derivatized dithiocarbamates alone are not immunogenic. The simple, easy and non-invasive ELISA methods for measurement of NO levels in body fluids will find a variety of uses, e.g., for diagnosis and monitoring of NO overprodn. that has been associated with many inflammatory and infectious diseases.

IT **85419-94-9**
(photoreactive crosslinking agent; antibodies directed against dithiocarbamates)
RN 85419-94-9 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



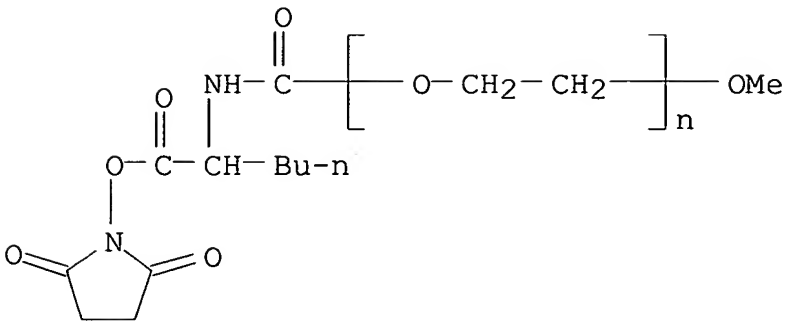
PAGE 1-B



IC ICM G01N033-566
ICS C07K016-00; A61K039-00; A61K039-38
CC 9-10 (Biochemical Methods)
IT 111-30-8, Glutaraldehyde 327-92-4, 1,5-Difluoro-2,4-dinitrobenzene 538-75-0, Dicyclohexylcarbodiimide 4856-87-5 5957-03-9, Bis(diazobenzidine) 13139-70-3, Dimethyl adipimidate 25952-53-8, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride 29878-26-0, Dimethyl suberimidate 36875-25-9, Heptanediimidic acid, dimethyl ester 53053-08-0, N-**Hydroxysuccinimidyl** 4-azidobenzoate 57683-72-4 57757-57-0, Dithiobis(succinimidyl propionate) 58626-38-3 59012-54-3, Dimethyl 3,3'-dithiobispropionimidate 59733-92-5 59733-94-7 60117-35-3 64987-85-5 65322-07-8, p-Azidophenylglyoxal 68181-17-9, N-Succinimidyl-3-(2-pyridyldithiopropionate) 68528-80-3, Disuccinimidyl suberate 72252-96-1 77658-91-4 79642-50-5 79886-55-8 80307-12-6 81069-02-5 82436-77-9, Bis(sulfosuccinimidyl) suberate **85419-94-9** 96602-46-9 102568-45-6 115616-51-8 118674-04-7 118790-78-6 141647-62-3

147492-84-0 160854-54-6 183006-87-3 184533-12-8 199804-21-2
199804-22-3 199804-23-4 199804-24-5 199804-25-6 199804-26-7
(photoreactive crosslinking agent; antibodies directed against dithiocarbamates)

L24 ANSWER 57 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 127:298636 HCA
TITLE: Branched and linear poly(ethylene glycol): influence of the polymer structure on enzymological, pharmacokinetic, and immunological properties of protein conjugates
AUTHOR(S): Veronese, Francesco M.; Caliceti, Paolo; Schiavon, Oddone
CORPORATE SOURCE: Dep. Pharmaceutical Sci., Centro Studio Chimica Farmaco Prodotti, Biologicamente Attivi CNR, Univ. Padova, Padua, 35131, Italy
SOURCE: Journal of Bioactive and Compatible Polymers (1997), 12(3), 196-207
CODEN: JBCPEV; ISSN: 0883-9115
PUBLISHER: Technomic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Linear and branched poly(ethylene glycol)s, with similar mol. wts., were conjugated with uricase and asparaginase, and an investigation of enzymol., and pharmacokinetic properties of the conjugates were carried out. The steric hindrance of the branched polymer has a relevant role in determining the biol. properties of the conjugates. Conjugations with branched polymers inactivate the enzyme less than the linear ones. Compared to the native and the linear polymer conjugate counterparts the branched polymer derivs.: (1) are more stable to proteolysis by elastase, pronase, and trypsin, (2) stay longer in the blood with increased systemic availability after i.v. administration in mice, and (3) give rise to lower levels of antinative enzyme antibodies after immunization. These data are consistent with a greater surface area of protein covered by the branched PEG.
IT **136372-28-6DP**, conjugates with proteins
(polymer structure effect on enzymol., pharmacokinetic, and immunol. properties of protein conjugates with branched and linear **PEG**)
RN 136372-28-6 HCA
CN Poly(oxy-1,2-ethanediyl), α-[[[(1S)-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]pentyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 15
IT 9002-12-4DP, Uricase, conjugates with PEG derivs. 9015-68-3DP, Asparaginase, conjugates with PEG derivs. 25322-68-3DP, PEG, derivs., conjugates with proteins **136372-28-6DP**, conjugates with proteins **159540-80-4DP**, conjugates with proteins
(polymer structure effect on enzymol., pharmacokinetic, and immunol. properties of protein conjugates with branched and linear **PEG**)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

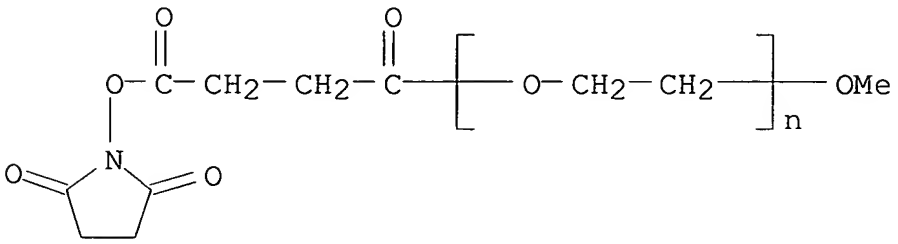
L24 ANSWER 58 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 127:210258 HCA
TITLE: Preparation of thermosensitive liposomes containing amphipathic polyethylene glycol for macromolecule delivery
AUTHOR(S): Yuda, Tsutomu; Pongpaibul, Yanee; Moribe, Kunikazu; Maruyama, Kazuo; Iwatsuru, Motoharu
CORPORATE SOURCE: Faculty Pharmaceutical Sciences, Teikyo University, Kanagawa, 199-01, Japan
SOURCE: Yakuzaigaku (1997), 57(2), 74-78
CODEN: YAKUA2; ISSN: 0372-7629
PUBLISHER: Nippon Yakuzai Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Long-circulating thermosensitive liposomes with hyperosmotic internal aqueous phase intended for the delivery of macromols. were prepared and characterized in vitro. Higher osmotic pressure markedly increased the release of macromols. such as dextran. This effect was pronounced with liposome containing amphipathic PEG. The release of
dextran was also influenced by the concentration of amphipathic PEG added

to the liposomes. These results indicate that higher internal osmotic pressure and amphipathic PEG content contributes to the in vitro temperature-dependent release of the macromol. dextran.

IT **78274-32-5**
(**preparation** of thermosensitive liposomes containing amphipathic **polyethylene glycol** for macromol. delivery)

RN 78274-32-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 63-5 (Pharmaceuticals)

IT 4537-76-2, Distearoylphosphatidylethanolamine 9004-54-0, Dextran, reactions **78274-32-5**
(**preparation** of thermosensitive liposomes containing amphipathic **polyethylene glycol** for macromol. delivery)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 59 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 126:268445 HCA

TITLE: Amphiphilic polyethylene glycol derivatives: long-circulating micellar carriers for therapeutic and diagnostic agents

AUTHOR(S): Torchilin, Vladimir P.; Trubetskoy, Vladimir S.

CORPORATE SOURCE: Center Imaging and Pharmaceutical Res., Harvard Med. Sch., Charlestown, MA, 02129, USA

SOURCE: Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (1997), 38(1), 545-546
CODEN: ACPPAY; ISSN: 0032-3934

PUBLISHER: American Chemical Society, Division of Polymer Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

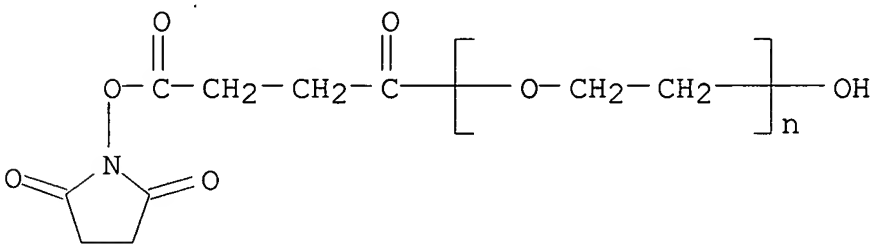
AB Amphiphilic AB-type copolymers form polymeric micelles with hydrophobic blocks making up the particle's core, while PEG blocks provide water solubility, long circulation time, and steric protection.

The small size of the micelles enhances permeability across physiol. barriers. Thus, PEG-PE (PE = phosphatidylethanolamine) conjugates (PEG mol. weight 2-12 kDa) formed stable micelles 18-50 nm in diameter in aqueous environments. These micelles incorporated the poorly water-soluble potential anticancer drug ellipticine. High drug:PEG ratios were obtained by use of hydrophobized drugs (e.g. rhodamine-PE, a fluorescent lipid probe). Micelles containing Gd-DTPA-PE or 111In-DTPA-PE were used in cutaneous lymphog. by MR imaging and γ-scintigraphy, resp. Fluorescein-labeled IgG was covalently linked to PEG-PE micelles via **activated** CO2H **groups** on PEG termini, illustrating the possibility of targeting micelles loaded with drugs or diagnostic agents. A methoxy-PEG/poly(Nε-triiodobenzoyl-L-lysine) copolymer formed 80-nm micelles with 44% I content in aqueous dispersion; these were used as a long-circulating contrast agent for computed tomog.

IT **102743-95-3D**, conjugates with phosphatidylethanolamines (micelles; amphiphilic polyethylene glycol derivs.: long-circulating micellar carriers for therapeutic and diagnostic agents)

RN 102743-95-3 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



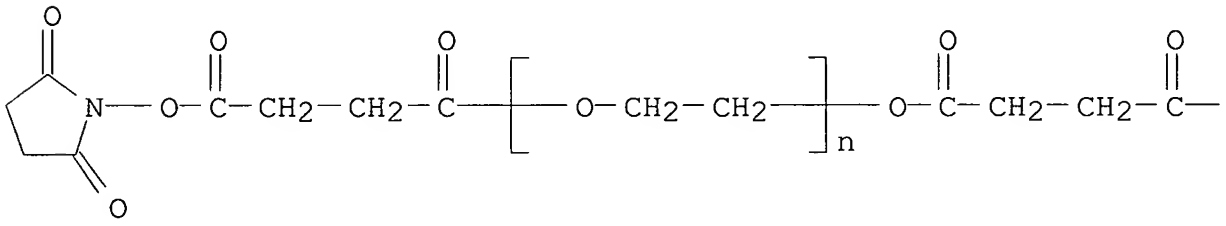
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 35

IT **102743-95-3D**, conjugates with phosphatidylethanolamines
188803-02-3D, conjugates with phosphatidylethanolamines (micelles; amphiphilic polyethylene glycol derivs.: long-circulating micellar carriers for therapeutic and diagnostic agents)

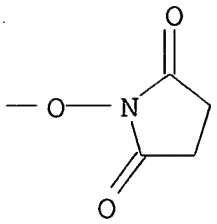
L24 ANSWER 60 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 126:242720 HCA
TITLE: Prolongation of the serum half-life period of superoxide dismutase by poly(ethylene glycol) modification
AUTHOR(S): Nakaoka, Ryusuke; Tabata, Yasuhiko; Yamaoka,

Tetsuji; Ikada, Yoshito
CORPORATE SOURCE: Research Center for Biomedical Engineering, Kyoto University, 53 Kawahara-cho Shogoin, Sakyo-ku, Kyoto, Japan
SOURCE: Journal of Controlled Release (1997), 46(3), 253-261
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Superoxide dismutase (SOD) was chemical modified using PEG with different mol. wts. to prepare PEG-SOD conjugates with different extents of modification. The body distribution of the conjugates i.v. injected to mice was investigated to assess the influence of modification on the serum half-life period of SOD. The SOD modification with PEG was effective in lowering the elimination rate of SOD from the blood circulation without any change in the distribution pattern of organs other than the kidney. The mol. weight of PEG used for modification and the modification extent have a min. effect on the half-life of the SOD. The half-life of the SOD and its PEG conjugates have a similar dependency on the apparent mol. weight as the PEG mols. This indicates that the half-life of SOD and the PEG conjugates are mainly determined by their mol. size.
IT **85419-94-9P**
(prolongation of serum half-life of superoxide dismutase by **PEG** modification)
RN 85419-94-9 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



CC 63-5 (Pharmaceuticals)
IT 37340-09-3P, Polyethylene glycol succinate **85419-94-9P**
(prolongation of serum half-life of superoxide dismutase by **PEG** modification)

L24 ANSWER 61 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 126:199966 HCA
TITLE: Manufacture of polyethylene glycol (PEG) monosubstituted with carboxyethyl- or carboxypropyl groups and their functional derivatives for biotechnical applications
INVENTOR(S): Harris, J. Milton; Kozlowski, Antoni
PATENT ASSIGNEE(S): Shearwater Polymers, Inc., USA; Harris, J. Milton; Kozlowski, Antoni
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9703106	A1	19970130	WO 1996-US11261	19960703
W: AL, AM, AT, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5672662	A	19970930	US 1995-642231	19951002
AU 9663457	A1	19970210	AU 1996-63457	

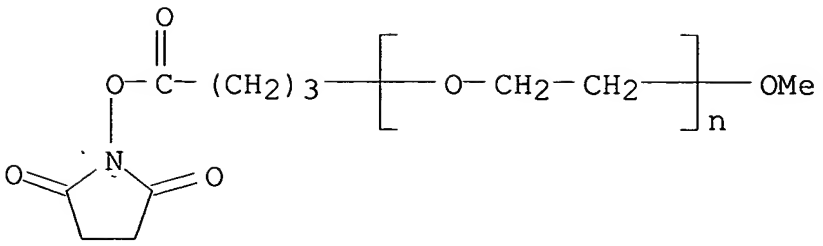
PRIORITY APPLN. INFO.: US 1995-499321 A 199507 07
US 1995-642231 A 199510 02
WO 1996-US11261 W 199607 03

AB Active esters of PEG-acids and related polymers are provided that have a single propionic or butanoic acid moiety and no other ester linkages. These esters have a half life in H2O of 10-25 min. For example, α-methoxy, ω-propionic acid succinimidyl ester of PEG ("methoxy-PEG-SPA") has a nearly ideal reactivity with NH2 groups on proteins and other biol. active substances. The half life of methoxy-PEG-SPA is .apprx.16.5 min in H2O. The invention also provides conjugates with proteins, enzymes, polypeptides, drugs, dyes, nucleosides, oligonucleotides, lipids, phospholipids, liposomes, and surfaces of solid materials that are compatible with living organisms, tissue, or fluid. For example, polyethylene glycol monomesylate was heated for 3 h under N with HSCH2CH2CO2Et in a EtOH/PhMe mixture containing NaOH and the product saponified with aqueous NaOH at room temperature to give HO(CH2CH2)nCH2CH2SCH2CH2CO2H. This was esterified with acryloyl chloride in CH2Cl2 in the presence of Et3N, the monoester esterified with N-hydroxysuccinimide in CH2Cl2 in the presence of N,N'-dicyclohexylcarbodiimide and the resulting active ester coupled with subtilisin.

IT **187848-51-7P**
(manufacture of **polyethylene glycol** monosubstituted with carboxyethyl- or carboxypropyl groups and their functional derivs. for biotech. applications)

RN 187848-51-7 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM C08G065-32
ICS A61K031-765
CC 35-8 (Chemistry of Synthetic High Polymers)
Section cross-reference(s): 1, 7, 9
IT 9001-78-9DP, Alkaline phosphatase, conjugate with α-methoxy-ω-succinimidooxycarbonylethylthioethyl-polyethylene glycol 9014-01-1DP, Subtilisin, conjugate with α-acryloyl-ω-succinimidooxycarbonylethylthioethyl-polyethylene glycol 117786-94-4P 174569-25-6DP, glass-bound 187848-48-2P **187848-51-7P** 187848-54-0P 187848-56-2P 187848-59-5P 187848-62-0P 187848-63-1P 187848-64-2P 187848-66-4P 187848-67-5P 187848-68-6P 187848-69-7P 187848-70-0P 187848-71-1P 187848-72-2P 187848-73-3DP, conjugate with subtilisin 187848-73-3DP, subtilisin conjugates
(manufacture of **polyethylene glycol** monosubstituted with carboxyethyl- or carboxypropyl groups and their functional derivs. for biotech. applications)

L24 ANSWER 62 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 126:6461 HCA
TITLE: Modified anti-ICAM-1 antibodies and their use in the treatment of inflammation
INVENTOR(S): Faanes, Ronald B.; Mc Goff, Paul E.; Shirley, Bret A.; Scher, David S.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA; Faanes, Ronald; McGoff, Paul; Shirley, Bret; Scher, David
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9634015	A1	19961031	WO 1996-US5550	

					19960423
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
US 5695760		A	19971209	US 1995-427355	19950424
IL 117993		A1	20000831	IL 1996-117993	19960421
AU 9655633		A1	19961118	AU 1996-55633	19960423
EP 822942		A1	19980211	EP 1996-912995	19960423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 11504516		T2	19990427	JP 1996-532624	19960423
ZA 9603287		A	19960813	ZA 1996-3287	19960424
TW 438809		B	20010607	TW 1996-85110360	19960826
PRIORITY APPLN. INFO.:				US 1995-427355 A	19950424
				WO 1996-US5550 W	19960423

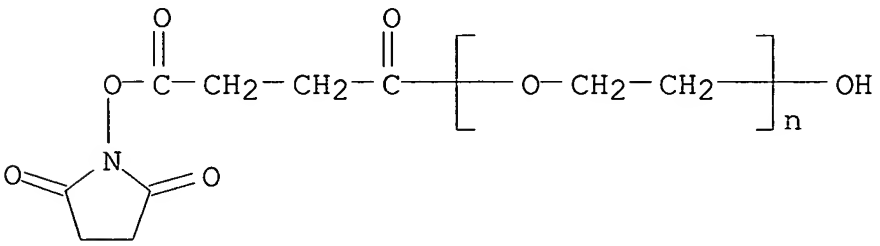
AB Methods for preventing or treating inflammation are provided. Specifically, such inflammation can be effectively treated or prevented through the use of anti-ICAM-1 antibodies which have been modified to contain poly(ethylene) glycol adducts. The modification reduces the immunoreactivity of the antibodies, and thus increases the antibodies' serum half life. Methods for forming, purifying and using such modified antibodies are described.

IT **102743-95-3**

(**polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)

RN 102743-95-3 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IC ICM C07K016-28
ICS C07K016-00; A61K039-395; A61K047-48; C07K001-20

CC 15-3 (Immunochemistry)

ST **polyethylene glycol** modified antibody ICAM1 inflammation

IT Intestine, disease
(Crohn's; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)

IT Cell adhesion molecules
(ICAM-1 (intercellular adhesion mol. 1); **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)

IT Kidney, disease
(acute glomerulonephritis; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)

IT Inflammation
(acute; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)

IT Respiratory distress syndrome
(adult; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)

IT Nervous system
Nervous system
(central, inflammation; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)

IT Toxicity
(cytokine-induced; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment

of inflammation)
IT Blood transfusion
(disorder, granulocyte transfusion-associated syndromes; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Dialysis
(hemodialysis; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Chromatography
(hydrophobic interaction; **polyethylene glycol** -modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Reperfusion
(injury; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Plasmapheresis
(leukapheresis; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Antibodies
(monoclonal; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Asthma
Autoimmune disease
Inflammation
Multiple organ failure
Multiple organ failure
Rhinovirus
Septicemia
Skin, disease
(**polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Antibodies
(**polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Polyoxyalkylenes, biological studies
(**polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Intestine, disease
(pseudomembranous enterocolitis; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Meningitis
(purulent, acute; **polyethylene glycol** -modified anti-ICAM-1 antibodies and their use in the treatment

of inflammation)
IT Arthritis
(reactive; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Burn
(thermal injury; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Cytokines
(toxicity; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Polymorphonuclear leukocyte
(transfusion associated syndromes; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Injury
(trauma; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT Intestine, disease
(ulcerative colitis; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT 7783-20-2, Ammonium sulfate, biological studies
(antibody purification; **polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)
IT 25322-68-3 **102743-95-3** 123502-58-9D, N-**Hydroxysuccinimidyl**
(**polyethylene glycol**-modified anti-ICAM-1 antibodies and their use in the treatment of inflammation)

L24 ANSWER 63 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 125:285010 HCA
TITLE: Method of preparing crosslinked polymeric biomaterial compositions for use in tissue augmentation
INVENTOR(S): Rhee, Woonza M.; Berg, Richard A.; Rosenblatt, Joel S.; Tefft, Jacqueline A.; Braga, Larry J.; Smestad, Thomas L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 14 pp., Cont.-in-part of U.S. Ser. No. 236,769.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5550187	A	19960827	US 1994-287549	19940808
US 5162430	A	19921110	US 1989-433441	19891114
US 5328955	A	19940712	US 1992-922541	19920730
US 5304595	A	19940419	US 1992-998802	19921230
US 5306500	A	19940426	US 1993-110577	19930823
US 5376375	A	19941227	US 1994-177578	19940105
US 5413791	A	19950509	US 1994-198128	19940217
US 5475052	A	19951212	US 1994-236769	19940502
US 5523348	A	19960604	US 1994-292415	19940818
US 5543441	A	19960806	US 1995-427576	19950424
US 5527856	A	19960618	US 1995-440274	19950512
US 5643464	A	19970701	US 1995-497573	19950630
EP 697218	A2	19960221	EP 1995-112218	19950803
EP 697218	A3	19960529		
R: DE, FR, GB, IT				
PRIORITY APPLN. INFO.:			US 1988-274071 B2	

			19881121
	US 1989-433441	A2	19891114
	US 1992-922541	A3	19920730
	US 1994-198128	A2	19940217
	US 1994-236769	A2	19940502
	US 1992-930142	A3	19920814
	US 1993-110577	A3	19930823
	US 1994-177578	A3	19940105
	US 1994-287549	A3	19940808
	US 1994-292415	A3	19940818
	US 1995-497573	A	19950630

AB The present invention discloses a novel method for preparing crosslinked biomaterial compns. for use in the augmentation of soft or hard tissue. In general, the method comprises mixing a biocompatible polymer, which is preferably collagen, with a sterile, dry crosslinking agent, which is preferably a synthetic hydrophilic

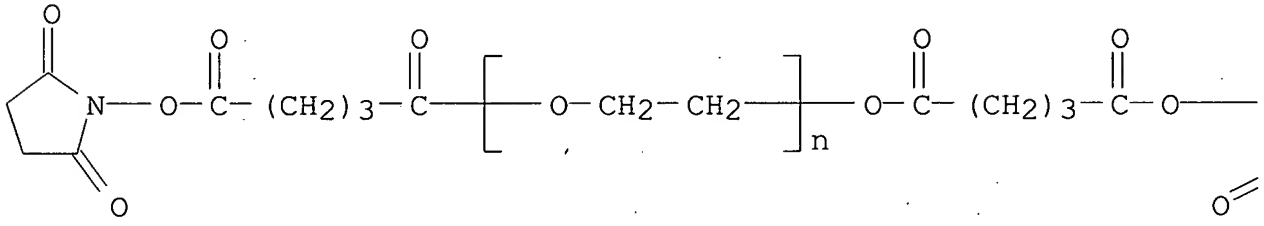
polymer such as a functionally activated polyethylene glycol. Also provided are preferred processes for preparing sterile, dry crosslinking agents contained within syringes for use in the method of the invention. Methods for sterilization of the crosslinking agent include, but are not limited to, sterile filtration, aseptic processing, and e-beam or gamma irradiation Methods for providing augmentation of soft or hard tissue using crosslinked biomaterial compns. prepared according to the method of the invention are also disclosed. A sterile, dry crosslinking agent was prepared by mixing 1500 mg of disfunctionally activated PEG succinimidyl glutarate with 150 mL of water for injection and filtration sterilization using a Durapore filter; 0.5 mL of solution obtained was aliquotted into each of 180 3 cc syringes and lyophilized.

IT **154467-38-6DP, Polyethylene glycol**
succinimidyl glutarate, reaction products with collagen
(**preparation** of biopolymers crosslinked with activated **polyethylene glycol** as implant biomaterial for tissue augmentation)

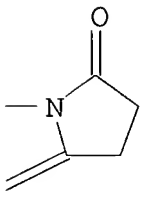
RN 154467-38-6 HCA

CN Poly(oxy-1,2-ethanediyl), α-[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]-ω-[[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IC C08G063-49; C08G063-91
NCL 525054100
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 38

IT 25322-68-3DP, derivs., reaction products with biopolymers
26403-72-5DP, reaction products with collagen 62066-14-2DP, reaction products with collagen 151709-76-1DP, Polyethylene glycol propion aldehyde, reaction products with collagen
154467-38-6DP, Polyethylene glycol succinimidyl glutarate, reaction products with collagen
155919-13-4DP, Polyethylene glycol succinimidyl carbonate, reaction products with collagen **159194-63-5DP**, reaction products with collagen **182677-57-2DP**, reaction products with collagen
(**preparation** of biopolymers crosslinked with activated **polyethylene glycol** as implant biomaterial for tissue augmentation)

IT 26403-72-5 62066-14-2 151709-76-1, Polyethylene glycol propion aldehyde **154467-38-6, Polyethylene glycol** succinimidyl glutarate 155919-13-4, Polyethylene glycol succinimidyl carbonate **159194-63-5 182677-57-2**
(**preparation** of biopolymers crosslinked with activated **polyethylene glycol** as implant biomaterial for tissue augmentation)

L24 ANSWER 64 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 125:160359 HCA
TITLE: Polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity
INVENTOR(S): De Polo, Nicholas J.; Hsu, David Chi-Tang
PATENT ASSIGNEE(S): Chiron Viagene, Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9621036	A2	19960711	WO 1995-US17005	199512 26

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT,

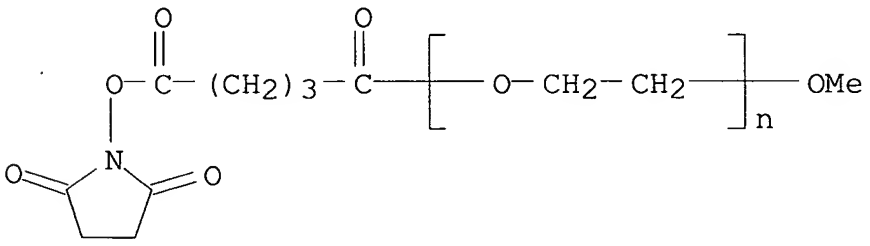
	SE			
AU 9646905	A1	19960724	AU 1996-46905	199512 26
PRIORITY APPLN. INFO.:			US 1994-366787	A 199412 30
			WO 1995-US17005	W 199512 26

AB Nucleic acid condensing agents with reduced immunogenicity are generated either by conjugation of polycations or by selection of basic amino acid regions from proteins. Conjugation involves a chemical linkage between a **polyalkylene glycol**, such as polyethylene glycol, or a polysaccharide, such as dextran, and a polycation. Addnl., gene delivery vehicles, such as viral vectors, may be conjugated with **polyalkylene glycol** or polysaccharide, to reduce their immunogenicity. Basic amino acid regions of proteins are identified by isoelec. point, and amino acid composition These condensing agents are complexed with nucleic acids and used to deliver agents to cells. Immunogenicity is assessed by whether neutralizing antibody is induced and by whether a serum component inactivates the complexes.

IT **111575-54-3P**
(preparation and conjugation with polycations of; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

RN 111575-54-3 HCA

CN Poly(oxy-1,2-ethanediyl), α-[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM C12N015-87
ICS A61K047-87

CC 3-1 (Biochemical Genetics)

IT Antibodies

Transferrins
(conjugates with DNA-polycation complexes for targeted delivery; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
(conjugates with polycations; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT Transformation, genetic
(polycationic complexes for delivery of nucleic acids in; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT Nucleic acids
(polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT Sialoglycoproteins
(asialo-, conjugates with DNA-polycation complexes for targeted delivery; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT Peptides, biological studies
(basic, conjugates, with **polyalkylene glycols** or polysaccharides; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT Histones
Protamines
(conjugates, with **polyalkylene glycols** or polysaccharides; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT Therapeutics
(geno-, polycationic complexes for delivery of nucleic acids in; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT Hemopoietins
(hematopoietic cell growth factors KL, conjugates with DNA-polycation complexes for targeted delivery; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT Lymphokines and Cytokines
(interleukins, conjugates with DNA-polycation complexes for

targeted delivery; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT Lipoproteins
(low-d., conjugates with DNA-polycation complexes for targeted delivery; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT 71-44-3D, Spermine, conjugates with **polyalkylene glycols** or polysaccharides 110-60-1D, Putrescine, conjugates with **polyalkylene glycols** or polysaccharides 124-20-9D, Spermidine, conjugates with **polyalkylene glycols** or polysaccharides 24937-47-1D, Polyarginine, conjugates with **polyalkylene glycols** or polysaccharides 24937-49-3D, Polyornithine, conjugates with **polyalkylene glycols** or polysaccharides 25104-12-5D, Polyornithine, conjugates with **polyalkylene glycols** or polysaccharides 25104-18-1D, Polylysine, conjugates with PEG 25212-18-4D, Polyarginine, conjugates with **polyalkylene glycols** or polysaccharides 38000-06-5D, Polylysine, conjugates with PEG
(as nucleic acid condensing agent; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT 11096-26-7, Erythropoietin 81627-83-0, M-CSF 83869-56-1, GM-CSF 143011-72-7, G-CSF
(conjugates with DNA-polycation complexes for targeted delivery; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT 9004-54-0DP, Dextran, conjugates with polycations 25322-68-3DP, conjugates with polycations
(polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT **111575-54-3P**
(preparation and conjugation with polycations of; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

IT 79934-70-6DP, conjugate with polylysine
(preparation of, as DNA condensing agent; polycationic conjugates of **polyalkylene glycols** or polysaccharides as nucleic acid condensing agents with reduced immunogenicity)

L24 ANSWER 65 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 124:105778 HCA

TITLE: An Adduct of cis-Diaminodichloroplatinum(II) and Polyethylene glycol-poly(L-lysine)-Succinate: Synthesis and Cytotoxic Properties

AUTHOR(S): Bogdanov, A. A., Jr.; Martin, C.; Bogdanova, A.; Brady, T. J.; Weissleder, R.

CORPORATE SOURCE: Department of Radiology, Massachusetts General Hospital, Boston, MA, 02129, USA

SOURCE: Bioconjugate Chemistry (1996), 7(1), 144-9
CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

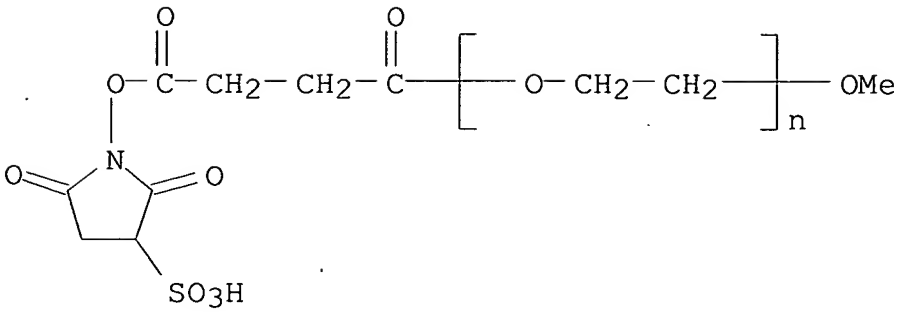
LANGUAGE: English

AB A noncovalent adduct of the antineoplastic drug cis-diaminodichloroplatinum (cDDP) and a biocompatible graft copolymer of poly(L-lysine) and methoxypolyethylene glycol succinate is described. Upon incubation of cDDP with [O-methylpolyethylene glycol-O'-succinyl]-N-ε-poly(L-lysine)n-N-ε-succinate (n = 250-270) highly soluble, long circulating adducts were formed which contained 4.3% of platinum by weight Approx. 60% of the polymer-associated drug was released during dialysis against saline or serum albumin containing saline, with a half-time of release of 63 h. The adducts showed a pronounced antineoplastic effect in BT-20 human adenocarcinoma cell cultures. In cell proliferation assays, the concentration of half-inhibition of [3H]thymidine uptake was 0.9 ± 0.2 μM for the drug-copolymer adduct compared to 0.3 ± 0.1 μM for free cDDP. The adduct showed a long blood half-life (ca. 14 h in rats) and accumulated in exptl. mammary adenocarcinomas at 2.5-3.5% injected dose per g of tissue. A control adduct of cDDP with the backbone portion of the copolymer, poly(L-lysine)-N-ε-succinate, had a short half-life in the bloodstream (ca. 30 min) and low accumulation (0.5% injected dose/g) in tumor. A dual therapeutic effect of methylpoly(ethylene glycol)succinylpoly(L-lysine)-succinate as a carrier of cDDP is suggested: (1) as a carrier for systemic release of the active drug from the macromol. while it circulates in the bloodstream and (2) as a carrier for on-site delivery which results from the release of the drug in the tumor as a consequence of accumulation of the copolymer in the tumor.

IT **172989-60-5P**
(in **preparation** of **PEG**-lysine graft copolymer)

RN 172989-60-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-3-sulfo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 1-6 (Pharmacology)
Section cross-reference(s): 37, 63
IT 31961-02-1P **172989-60-5P**
(in **preparation** of **PEG**-lysine graft copolymer)

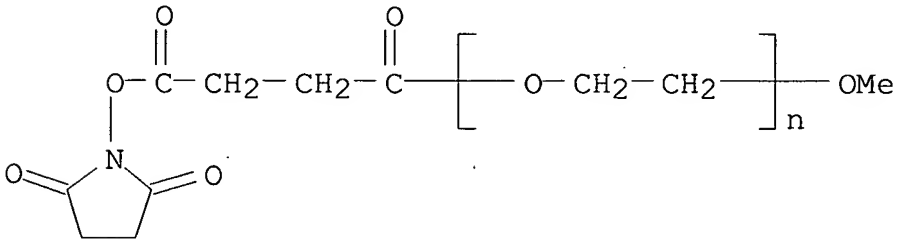
L24 ANSWER 66 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 123:17579 HCA
TITLE: Polyethylene glycol modification of interleukin-6 enhances its thrombopoietic activity
AUTHOR(S): Tsutsumi, Yasuo; Kihira, Tetsunari; Tsunoda, Shin-ichi; Okada, Naoki; Kaneda, Yoshihisa; Ohsugi, Yoshiyuki; Miyake, Masaharu; Nakagawa, Shinsaku; Mayumi, Tadanori
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka, 565, Japan
SOURCE: Journal of Controlled Release (1995), 33(3), 447-51
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study was conducted to increase the in vivo thrombopoietic activity of interleukin-6 (IL-6). Recombinant human IL-6 was covalently conjugated with N-succinimidyl succinate monomethoxy polyethylene glycol (PEG). The in vitro bioactivity of the PEG-modified IL-6 was reduced with increase in its degree of PEG modification, but the in vivo thrombopoietic activity of PEG-modified IL-6 was markedly increased compared to unmodified IL-6. In particular, modified IL-6, in which 54% of the 14 lysine amino groups were coupled with PEG, showed >10 times greater thrombopoietic effect in vivo than unmodified IL-6. The area under the serum concentration curve of PEG-modified IL-6 after s.c. injection was
>17 times larger than that of unmodified IL-6. Chemical attachment of

PEG to IL-6 thus increased the bioavailability of IL-6, and may facilitate its potential therapeutic use.

IT **78274-32-5DP**, reaction products with interleukin-6 (thrombopoietic effects of **PEG**-modified interleukin-6)

RN 78274-32-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 63-3 (Pharmaceuticals)

IT **78274-32-5DP**, reaction products with interleukin-6 (thrombopoietic effects of **PEG**-modified interleukin-6)

L24 ANSWER 67 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 122:89211 HCA

TITLE: Strategies for covalent attachment of doxorubicin to poly(PEG-Lys), a new water-soluble poly(ether urethane)

AUTHOR(S): Nathan, Aruna; Zalipsky, Samuel; Kohn, Joachim

CORPORATE SOURCE: Department of Chemistry, Rutgers University, New Brunswick, NJ, 08903, USA

SOURCE: Journal of Bioactive and Compatible Polymers (1994), 9(3), 239-51
CODEN: JBCPEV; ISSN: 0883-9115

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Poly(PEG-Lys) is a new, water soluble poly(ether urethane) that has shown promise as an injectable drug carrier. To evaluate the possible use of this drug carrier in chemotherapy, three different approaches for the covalent attachment of doxorubicin to the pendent carboxylic acid groups of poly(PEG-Lys) were developed. In one approach, the pendent carboxylic acid groups of poly(PEG-Lys) were converted to N-hydroxysuccinimide active esters, which spontaneously formed hydrolytically stable amide bonds upon reaction with the amino group located on the daunosamine ring of doxorubicin. The amount of amide-bound doxorubicin was about 7.3 mg/100 mg of conjugate. In a second approach, the degradable hydrazone linkage was formed by reaction of the polymeric hydrazide derivative of poly(PEG-Lys), designated as poly(PEG-Lys hydrazide), with the 13-keto group of doxorubicin. After purification, the amount of

carrier-bound doxorubicin was 13.5 mg/100 mg of conjugate. In the third approach, the conjugation of doxorubicin via secondary amine linkages was explored. In this approach, the aldehyde derivative of poly(PEG Lys), designated as poly(PEG-Lys-aldehyde), was reacted with doxorubicin, followed by reduction of the intermediate Schiff base with sodium cyanoborohydride. After extensive purification of the carrier, the amount of bound doxorubicin was 10 mg/100 mg of conjugate. All conjugates were characterized by UV/Vis and FTIR spectroscopy and by thin layer chromatog. The conjugates were free of detectable contamination by unbound drug.

IT **160175-58-6DP**, doxorubicin conjugates
(**preparation** of doxorubicin-poly(**PEG**-Lys) conjugates for drug delivery)

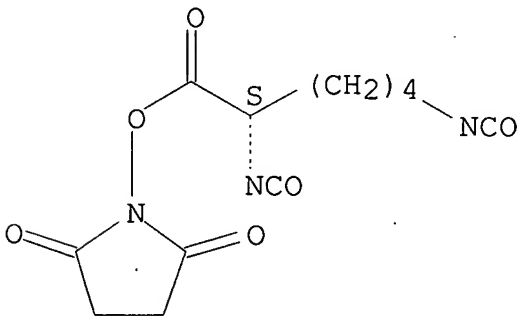
RN 160175-58-6 HCA

CN 2,5-Pyrrolidinedione, 1-[(2,6-diisocyanato-1-oxohexyl)oxy]-, (S)-, polymer with α-hydro-ω-hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM 1

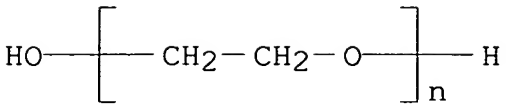
CRN 160175-57-5
CMF C12 H13 N3 O6

Absolute stereochemistry.



CM 2

CRN 25322-68-3
CMF (C2 H4 O)n H2 O
CCI PMS



CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 35
IT 23214-92-8DP, Doxorubicin, conjugates with poly(PEG-Lys)
160175-58-6DP, doxorubicin conjugates 160175-60-0DP, doxorubicin conjugates 160175-62-2DP, doxorubicin conjugates 160383-04-0DP, doxorubicin conjugates
(**preparation** of doxorubicin-poly(**PEG**-Lys) conjugates for drug delivery)

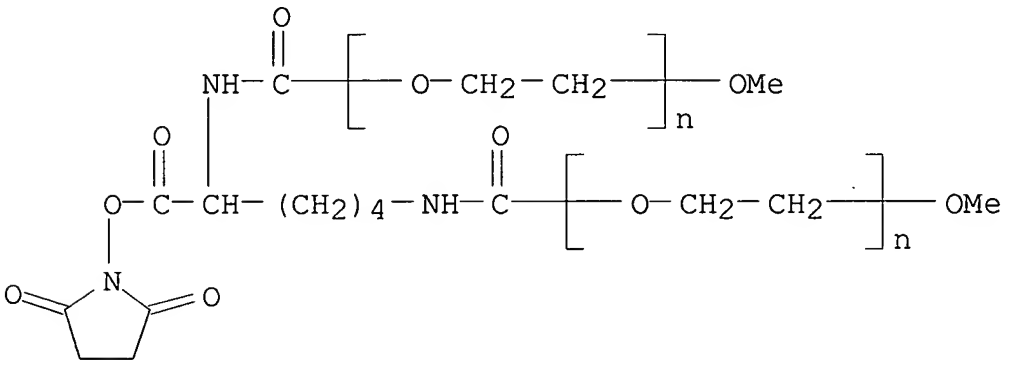
L24 ANSWER 68 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 122:75898 HCA
TITLE: A Branched Monomethoxypoly(ethylene glycol) for Protein Modification
AUTHOR(S): Monfardini, Cristina; Schiavon, Oddone; Caliceti, Paolo; Morpurgo, Margherita; Harris, J. Milton; Veronese, Francesco M.
CORPORATE SOURCE: Centro di Studio di Chimica del Farmaco e dei Prodotti Biologicamente, University of Padua, Padua, 35131, Italy
SOURCE: Bioconjugate Chemistry (1995), 6(1), 62-9
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Procedures are described for linking monomethoxypoly(ethylene glycol) (mPEG) to both ε and α amino groups of lysine. The lysine carboxyl **group** can then be **activated** as a succinimidyl ester to obtain a new mPEG derivative (mPEG2-COOSu) with improved properties for biotech. applications. This branched reagent showed in some cases a lower reactivity toward protein amino groups than the linear mPEG from which it was derived. A comparison of mPEG- and mPEG2-modified enzymes (RNase, catalase, asparaginase, trypsin) was carried out for activity, pH and temperature stability, Km and Kcat values, and protection to proteolytic digestion. Most of the adducts from mPEG and mPEG2 modification presented similar activity and stability toward temperature change and pH change, although in a few cases mPEG2 modification was found to increase temperature stability and to widen the range of pH stability of the adducts. All of the enzymes modified with the branched polymer presented greater stability to proteolytic digestion relative to those

modified with the linear mPEG. A further advantage of this branched mPEG lies in the possibility of a precise evaluation of the number of polymer mols. bound to the proteins; upon acid hydrolysis, each mol. of mPEG2 releases a mol. of lysine which can be detected by amino acid anal. Finally, dimerization of mPEG by coupling to lysine provides a needed route to monofunctional PEGs of high mol. weight

IT **159540-80-4P**
(branched monomethoxy **polyethylene glycol** for protein modification)

RN 159540-80-4 HCA

CN Poly(oxy-1,2-ethanediyl), α,α'-[[(1S)-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-1,5-pentanediyl]bis(iminocarbonyl)]bis[.omega.-methoxy- (9CI) (CA INDEX NAME)



CC 9-14 (Biochemical Methods)
Section cross-reference(s): 6, 7, 16

IT 124661-64-9P 159540-78-0P 159540-79-1P **159540-80-4P**
(branched monomethoxy **polyethylene glycol** for protein modification)

L24 ANSWER 69 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 121:249508 HCA

TITLE: Lyophilized polyethylene oxide-modified catalase composition, polypeptide complexes with cyclodextrin and treatment of diseases with the catalase compositions

INVENTOR(S): Phillips, Christopher P.; Snow, Robert A.

PATENT ASSIGNEE(S): Sterling Winthrop Inc., USA

SOURCE: U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 178,205.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5334382	A	19940802	US 1994-195945	19940210
US 5298410	A	19940329	US 1993-23182	19930225
US 5389381	A	19950214	US 1994-178205	19940105
PRIORITY APPLN. INFO.:			US 1993-23182 A3	19930225
			US 1994-178205 A2	19940105

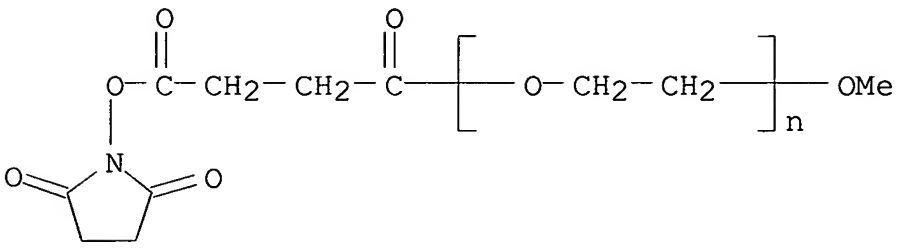
AB A lyophilized catalase composition with improved properties comprises a catalase conjugate with "low-diol" PEG and a cyclodextrin. The cyclodextrin acts as a cryoprotectant which prevents catalase aggregation. Preparation of catalase-PEG conjugates using low-diol PEG (i.e. PEG containing, on average, only one free hydroxyl) results in conjugates with better serum half-life and lower immunogenicity. The lyophilized PEG-catalase composition is prepared by carboxylating monomethoxy-PEG (i.e. the diol content of the monomethoxy-PEG is <10%), esterifying the carboxy group, reacting the catalase and activated PEG, preparing a solution of PEG-catalase and cyclodextrin, and lyophilizing the solution Reconstitution of the lyophilized catalase composition provides a solution which can be used in parenteral therapy for treatment of disease conditions caused by H2O2, such as inflammation, ischemia, reperfusion damage, trauma, and stroke. Methods of preparing low-diol or zero-diol monomethoxy-PEG and derivs. thereof, use of these derivs. to prepare numerous PEG conjugates, and improved shelf-life of the compns. were demonstrated.

IT **78274-32-5DP**, low- or zero-diol
(**preparation** and reaction of, in **preparation** of enzyme-**PEG** conjugate with improved immunogenicity and serum half-life)

RN 78274-32-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-

1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM C12N009-96
ICS A61K031-715; A61K037-26
NCL 424094300
CC 7-3 (Enzymes)
Section cross-reference(s): 1, 9, 63
IT 9004-74-4DP, low- or zero-diol 31961-02-1DP, low- or zero-diol
78274-32-5DP, low- or zero-diol
(**preparation** and reaction of, in **preparation** of enzyme-**PEG** conjugate with improved immunogenicity and serum half-life)

L24 ANSWER 70 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 120:280281 HCA
TITLE: Biocompatible polymers containing diagnostic or therapeutic moieties
INVENTOR(S): Bogdanov, Alexei A.; Brady, Thomas J.
PATENT ASSIGNEE(S): General Hospital Corp., USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

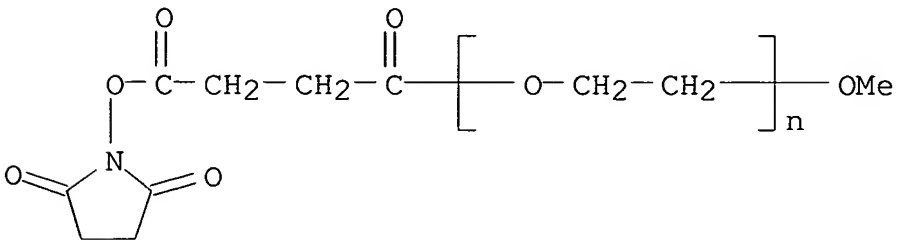
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9405203	A1	19940317	WO 1993-US7880	19930823
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9350857	A1	19940329	AU 1993-50857	19930823

				23
EP 665729	A1	19950809	EP 1994-908874	199308 23
EP 665729	B1	20030507		
R: DE, ES, FR, GB, IE, IT				
JP 08501097	T2	19960206	JP 1994-507247	199308 23
ES 2199226	T3	20040216	ES 1994-908874	199308 23
US 5871710	A	19990216	US 1996-738177	199610 28
PRIORITY APPLN. INFO.:			US 1992-940590 A	199209 04
			WO 1993-US7880 W	199308 23
			US 1994-250635 A2	199405 27
			US 1994-267150 B1	199406 27

AB A biocompatible medical composition includes a polymeric carrier, a protective chain linked to the polymeric carrier, and a reporter group linked to the carrier or to the carrier and the protective chain. The invention also relates to a composition for treating a disease in a patient by administering a therapeutically effective amount of the composition, and may include scanning the patient using an imaging technique which can detect the reporter group to obtain a visible image of the distribution of the composition The composition shows an extended blood half-life, low toxicity, and nonimmunogenicity. For example, methoxypolyethylene glycol-polylysine-diethylenetriamine pentaacetic acid-Gd(III) compound was prepared and i.v. injected to a cat. MR images of the head of the cat provided 3-D bright pixel reconstructions of vessel maps with high vessel/background signal ratio, eliminating the need for background subtraction.

IT **78274-32-5P**

(preparation and reaction of, with polylysine and DTPA)
RN 78274-32-5 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM A61B005-055
ICS C07H023-00; A61K037-14; A61K031-715; A61K049-02
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 8, 9
IT 25322-68-3, **PEG** 37286-64-9, Methoxy **polypropylene glycol**
(as protective chain for polyamino acid carrier in preparation of drug
conjugates for target delivery or diagnostic imaging)
IT **78274-32-5P**
(preparation and reaction of, with polylysine and DTPA)
IT 67-43-6DP, Diethylenetriamine pentaacetic acid, reaction products with **PEG** ester and polylysine and gadolinium
7440-54-2DP, Gadolinium, reaction products with **PEG** ester-polylysine-DTPA 9004-74-4DP, Methoxy **Polyethylene glycol**, reaction products with polylysine and DTPA and gadolinium 15750-15-9DP, Indium (111), reaction products with **PEG** ester-polylysine-DTPA, preparation 25104-18-1DP, Poly(L-lysine), reaction products with **PEG** ester and DTPA and gadolinium 38000-06-5DP, Poly(L-lysine), reaction products with **PEG** ester and DTPA and gadolinium
(preparation of, as imaging contrast agent)
IT 6066-82-6, N-Hydroxysuccinimide
(reaction of, with **PEG** Me ester succinate)
IT 25104-18-1, Poly(L-lysine) 38000-06-5, Poly(L-lysine)
(reaction of, with **PEG** Me ester succinyl-N-**hydroxysuccinimidyl** ester and DTPA)
IT 10138-52-0, Gadolinium chloride
(reaction of, with **PEG** ester-polylysine-DTPA)
IT 110-15-6, Butanedioic acid, reactions
(reaction of, with **PEG** monomethyl ester)
IT 23911-26-4, DTPA cyclic anhydride
(reaction of, with polylysine and **PEG** monomethyl ester derivative)

IT 9004-74-4, Methoxy **Polyethylene glycol**
(reaction of, with succinic acid)

L24 ANSWER 71 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 120:264829 HCA
TITLE: Crosslinked protein or polysaccharide hydrogels, their preparation, and their use in imaging and therapy
INVENTOR(S): Weissleder, Ralph; Bogdanov, Alexei
PATENT ASSIGNEE(S): General Hospital Corp., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9403155	A1	19940217	WO 1993-US7314	19930804
W: CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5514379	A	19960507	US 1992-927068	19920807
PRIORITY APPLN. INFO.:			US 1992-927068 A	19920807

AB Biocompatible, biodegradable hydrogels are prepared from a backbone compound (proteins and polysaccharides, e.g., albumin, polymannuronic acid, or polygalacturonic acid.) bonded to a crosslinking agent. Suitable crosslinking agents include polyvalent derivs. of polyethylene or **polyalkylene glycol**. These hydrogel compns. may be loaded with diagnostic labels, e.g., radiopaque, paramagnetic, or superparamagnetic materials, or therapeutic drugs, e.g., chemotherapeutic drugs, antibiotics, or cells that produce therapeutic agents. Such hydrogels are used for imaging, treatment, and embolization. Bis(N-**hydroxysuccinimidyl)polyethylene glycol** disuccinate was prepared and reacted with bovine serum albumin (BSA) and Gd-DTPA-BSA to form a paramagnetic hydrogel. The hydrogel was implanted in rats and the dissoln. was observed by repeated magnetic resonance imaging. Peritoneally implanted samples degraded faster

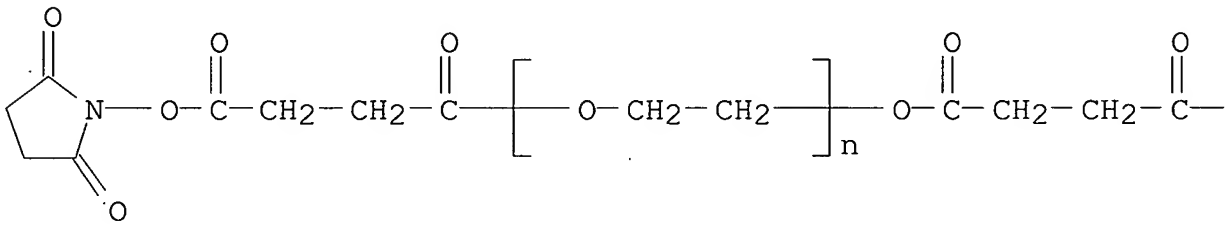
than i.m. implanted samples.

IT **85419-94-9P**
(preparation and reaction of, with albumin and albumin-gadolinium DTPA
conjugate, in preparation of paramagnetic hydrogel)

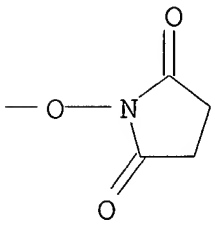
RN 85419-94-9 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IC ICM A61K009-10

CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 63

ST hydrogel protein polysaccharide crosslinking agent imaging; albumin **PEG** gadolinium hydrogel MRI; therapy hydrogel protein polysaccharide

IT Neoplasm, toxic chemical and physical damage
(embolization of, with hydrogel of **PEG** derivative-crosslinked albumin)

IT 9002-98-6D, Polyethyleneimine, reaction products with crosslinking agent 9004-54-0D, Dextran, derivs., reaction products with crosslinking agent 9005-25-8D, Starch, derivs., reaction products with crosslinking agent 9046-38-2D, Polygalacturonic acid, reaction products with crosslinking agent 25322-68-3D, Polyoxyethylene glycol, derivs., reaction products with protein or polysaccharide backbone 25322-68-3D, **Polyethylene**

glycol, halide- and benzoxazole-terminated derivs., reaction products with crosslinking agent 25322-69-4D, **Polypropylene glycol**, derivs., reaction products with protein or polysaccharide backbone 29894-36-8D, Polymannuronic acid, reaction products with crosslinking agent 35625-91-3D, reaction products with protein or polysaccharide backbone 154623-96-8D, reaction products with protein or polysaccharide backbone 154623-97-9D, reaction products with protein or polysaccharide backbone 154623-98-0D, reaction products with protein or polysaccharide backbone 154623-99-1D, reaction products with protein or polysaccharide backbone 154624-00-7D, reaction products with protein or polysaccharide backbone
(biocompatible and biodegradable hydrogel containing, for imaging and therapy)

IT 9005-38-3, Sodium alginate
(paramagnetic hydrogel containing bivalent **PEG** derivative-crosslinked)

IT 37684-51-8P, **Polyethylene glycol** disuccinate
(preparation and reaction of, in preparation of paramagnetic hydrogel)

IT **85419-94-9P**
(preparation and reaction of, with albumin and albumin-gadolinium DTPA conjugate, in preparation of paramagnetic hydrogel)

IT 20694-16-0DP, Gadolinium-DTPA, reaction products with albumin and **PEG** derivative
(preparation of, as paramagnetic hydrogel)

IT 108-30-5, Succinic anhydride, reactions
(reaction of, with **PEG**)

IT 25322-68-3, **Polyethylene glycol**
(reaction of, with succinic anhydride)

L24 ANSWER 72 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 119:19590 HCA
TITLE: Determination of N-**hydroxysuccinimidyl** -activated **polyethylene glycol** esters by gel permeation chromatography with post-column alkaline hydrolysis
AUTHOR(S): Shah, Bhavana; Watson, Eric
CORPORATE SOURCE: Amgen Cent., Amgen Inc., Thousand Oaks, CA, 91320-1789, USA
SOURCE: Journal of Chromatography (1993), 629(2), 398-400
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English

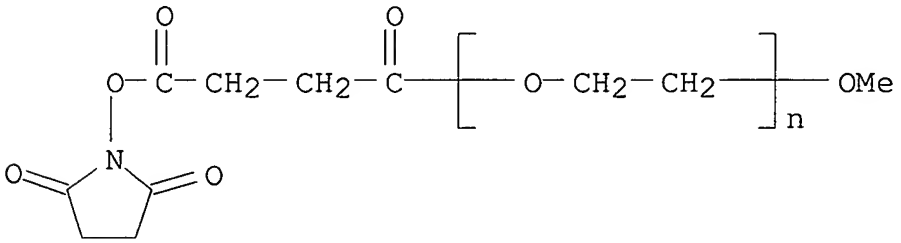
AB An HPLC method is reported for the determination of N-

hydroxysuccinimidyl-activated **polyethylene glycol** ester. The activated **polyethylene glycol** sample is first separated by size-exclusion chromatog. on a polymeric column with THF as the eluent, and after elution is subjected to post-column online hydrolysis with 0.1M sodium hydroxide. Liberation of N-hydroxysuccinimide occurs rapidly and is monitored by UV detection at 266 nm. The amount released is determined from a standard curve generated from free N-hydroxysuccinimide and used to calculate the concentration of active ester initially present.

IT **78274-32-5**
(determination of, by gel permeation chromatog. with post-column alkaline hydrolysis)

RN 78274-32-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 80-6 (Organic Analytical Chemistry)
Section cross-reference(s): 9

ST **hydroxysuccinimidyl** activated **polyethylene glycol** ester detn; gel chromatog activated **polyethylene glycol** ester

IT 25322-68-3D, **Polyethylene glycol**, esters, **hydroxysuccinimidyl**-activated **78274-32-5**
(determination of, by gel permeation chromatog. with post-column alkaline hydrolysis)

L24 ANSWER 73 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 116:169599 HCA

TITLE: Accurate evaluation method of the polymer content in monomethoxy(polyethylene glycol) modified proteins based on amino acid analysis

AUTHOR(S): Sartore, Luciana; Caliceti, Paolo; Schiavon, Oddone; Monfardini, Cristina; Veronese, Francesco M.

CORPORATE SOURCE: Cent. Stud. Chim. Farm. Prod. Biologicamente

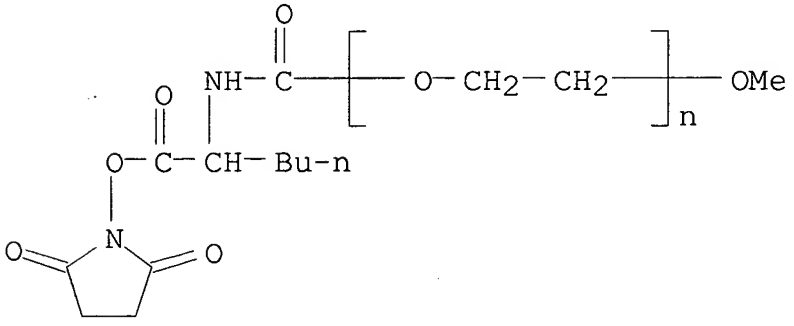
Attivi, Univ. Padova, Padua, 351000, Italy
SOURCE: Applied Biochemistry and Biotechnology (1991), 31(3), 213-22
CODEN: ABIBDL; ISSN: 0273-2289
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To overcome the uncertainty of the colorimetric or fluorimetric method so far employed for the evaluation of monomethoxy(polyethylene glycol) (MPEG) covalently bound to protein, a direct method based on amino acid anal. is proposed. The method exploits the use of MPEG, which was bounded with the unnatural amino acid norleucine (MPEG-Nle). MPEG-Nle was **activated** at its carboxylic **group** to succinimidyl ester for the binding to the amino groups of protein. After acid hydrolysis, the amino acid content is evaluated by conventional amino acid analyzer or by reverse-phase HPLC as phenylthiocarbamyl derivative The number of bound MPEG chains is calculated from the amino acid composition, since one norleucine residue is released from each bound polymer chain. The method was verified with several proteins in comparison with colorimetric ones, also in the case of proteins that contain chromophores in the visible range, such cytochrome c. It was observed that in most of the cases, the colorimetric methods give an overestimation of the degree of protein modification.

IT **136372-28-6P**
(preparation and reaction with protein)

RN 136372-28-6 HCA

CN Poly(oxy-1,2-ethanediyl), α-[[[(1S)-1-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]pentyl]amino]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)



CC 9-16 (Biochemical Methods)
Section cross-reference(s): 6

IT **136372-28-6P**
(preparation and reaction with protein)

L24 ANSWER 74 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 114:22373 HCA
TITLE: Human granulocyte colony-stimulating factor and its modification with **PEG**
INVENTOR(S): Ishikawa, Rika; Okada, Yuji; Kakitani, Makoto
PATENT ASSIGNEE(S): Kirin-Amgen, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9006952	A1	19900628	WO 1989-JP1292	19891222
W: JP, US RW: AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, SE				
EP 401384	A1	19901212	EP 1990-900360	19891222
EP 401384	B1	19960313		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
AT 135370	E	19960315	AT 1990-900360	19891222
US 5824778	A	19981020	US 1992-983620	19921130
US 6166183	A	20001226	US 1997-957719	19971027
US 2002177688	A1	20021128	US 2001-921114	20010802
US 2003204057	A1	20031030	US 2003-436784	20030512
US 2004158041	A1	20040812	US 2004-750797	20040102
US 2004204566	A1	20041014	US 2004-751242	20040102

PRIORITY APPLN. INFO.: JP 1988-324747 A

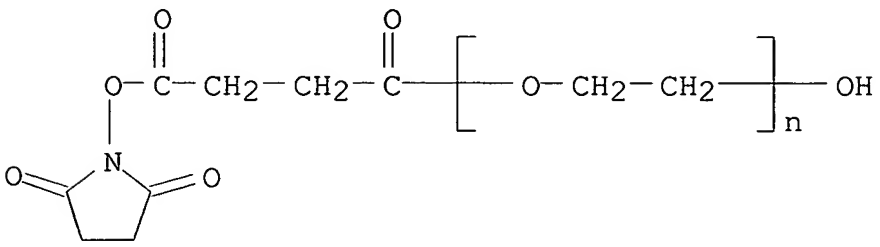
			19881222
	JP 1989-199176	A	19890731
	US 1989-566451	B1	19891222
	WO 1989-JP1292	W	19891222
	US 1990-566451	B1	19901001
	US 1992-983620	A1	19921130
	US 1997-957719	A1	19971027
	US 2000-518896	B1	20000306
	US 2001-921114	A3	20010802

AB Recombinant human granulocyte colony-stimulating factor (G-CSF) is modified with **PEG** to prolong its in vivo activity and to improve its neutrophil growth-activating activity. G-CSF modified with activated **PEG** 4500 (N-**hydroxysuccinimidyl-PEG**) (10 μg/kg i.v.) stimulated the peripheral neutrophil number in mice to 20.8 + 102/μL, as compared to 9.6 + 102 and 5.6 + 102/μL, resp., for natural CSF and the vehicle control. The half-life of the CSF modified with **PEG** 10,000 in male rats was 7.05 h vs. 1.79 h for natural CSF.

IT **102743-95-3DP**, reaction products with colony-stimulating factor
(preparation and neutrophil growth-activating activity of)

RN 102743-95-3 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IC ICM C07K013-00
ICS C07K003-08; A61K037-02
CC 15-5 (Immunochemistry)
Section cross-reference(s): 1, 9
ST colony stimulating factor **PEG** modification
IT Neutrophil
(proliferation of, recombinant human granulocyte colony-stimulating factor modified with **PEG** effect on)
IT 25322-68-3DP, **PEG**, reaction products with colony-stimulating factor 34901-14-9DP, reaction products with colony-stimulating factor 62683-29-8DP, Colony stimulating factor, reaction products with **PEG** 72708-10-2DP, reaction products with colony-stimulating factor 102484-11-7DP, Colony-stimulating factor (human clone pBRV-2 protein moiety reduced), reaction products with **PEG 102743-95-3DP**, reaction products with colony-stimulating factor 110908-59-3DP, reaction products with **PEG**
(preparation and neutrophil growth-activating activity of)

L24 ANSWER 75 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 110:101773 HCA
TITLE: Modification of tissue plasminogen activating factor with polyethylene glycol alkyl ethers for improvement of bioavailability
INVENTOR(S): Ajisaka, Katsumi; Yokota, Itsuro; Hamaguchi, Yoshitaka; Nishida, Hiroko
PATENT ASSIGNEE(S): Meiji Milk Products Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 63060938 A2 19880317 JP 1986-205201 198609 02

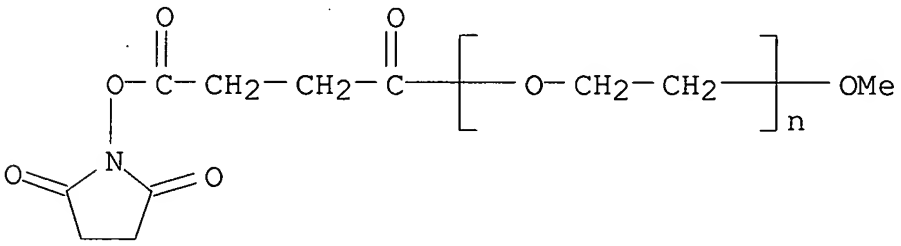
PRIORITY APPLN. INFO.: JP 1986-205201 198609 02

AB R1(OCH2CH2)nOH (R1 = C1-5 alkyl; n = 40-140) is bound to NH2 **groups** of tissue plasminogen **activating** factor (I) to increase bioavailability of I. I (mol. weight about 70,000, 3995 IU/mL) (75 mL) was dialyzed overnight at 4° against 1M K3PO4 buffer (pH 7.5), and treated 2 h at 4° with 2.4g polyethylene glycol bound to N-hydroxysuccinimide. The reaction solution was then dialyzed against 10 mM phosphate buffer (pH 7.5) containing 0.15M NaCl, and concentrated Polyethylene glycol-I complexes were i.v. injected to rabbits and the long-lasting bioavailability was demonstrated.

IT **78274-32-5**
(plasminogen activator modification with)

RN 78274-32-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC ICM A61K037-02
ICS C12N009-64

CC 63-5 (Pharmaceuticals)

IT **78274-32-5**
(plasminogen activator modification with)

L24 ANSWER 76 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 105:12188 HCA

TITLE: Preparation of hemoglobin-**polyalkylene glycol** complexes as blood substitutes

INVENTOR(S): Iwasaki, Takaharu; Iwashita, Yuji

PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan; Fujirebio, Inc.

SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF

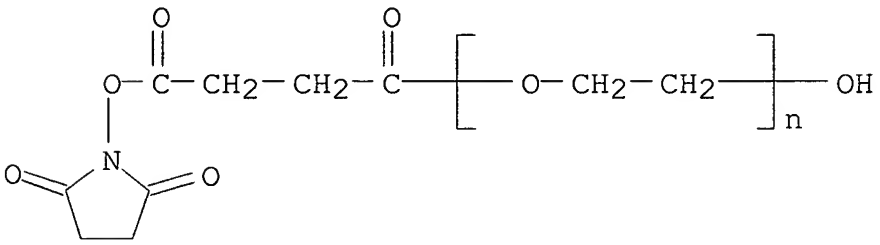
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61053223	A2	19860317	JP 1984-174351	19840822
JP 05064128	B4	19930914		

PRIORITY APPLN. INFO.: JP 1984-174351 19840822

AB Hb-**polyalkylene glycol** complexes are prepared by treating Hb with carboxyl-containing **polyalkylene glycol** in the presence of amino acids. These complexes are effective as O carriers or blood substitutes. Thus, Hb isolated from human erythrocytes was treated with polyethylene glycol succinimidyl succinate in the presence of glycine to give a blood substitute.

IT **102743-95-3D**, Hb complexes
(blood substitutes)
RN 102743-95-3 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IC ICM A61K037-14
ICA A61K035-18
CC 63-7 (Pharmaceuticals)
ST **polyalkylene glycol** Hb blood substitute
IT Amino acids, biological studies
(Hb treatment with carboxyl-containing **polyalkylene glycol** in presence of)
IT 56-40-6, biological studies
(Hb treatment with carboxyl-containing **polyalkylene glycol** in presence of)

IT **102743-95-3D**, Hb complexes
(blood substitutes)

L24 ANSWER 77 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 104:182652 HCA
TITLE: Activation of Trisacryl gels with chloroformates and their use for affinity chromatography and protein immobilization
AUTHOR(S): Miron, T.; Wilchek, M.
CORPORATE SOURCE: Dep. Biophys., Weizmann Inst. Sci., Rehovot, Israel
SOURCE: Applied Biochemistry and Biotechnology (1985), 11(6), 445-56
CODEN: ABIBDL; ISSN: 0273-2289
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The activation is described with chloroformates of Trisacryl GF 2000, a new synthetic gel support that is stable, hydrophilic, and contains large amts. of hydroxyl **groups** available for **activation**. Of all the reagents tested, activation with N-hydroxysuccinimide chloroformate and p-nitrophenyl chloroformate in organic solvents provides the best activation yield and subsequent coupling. When Trisacryl was activated in Me2CO with the chloroformates in the presence of 4-dimethylaminopyridine as base and catalyst, up to 30% of the hydroxyl groups (i.e., 1/repeating unit) could be activated. Amino-containing ligands and protein were coupled to these carriers at pH 8 or higher. For better results in affinity-chromatog. applications, spacers of ε-aminocaproic acid or diaminohexane were introduced. The efficacy of these columns was demonstrated by purification of enzymes, antibodies, and antigens. The performance of these new columns were compared with that of Sepharose columns activated in various ways. In every case, the properties of the Trisacryl support proved superior with particular reference to the purity of the product obtained.

IT **102038-53-9P**
(preparation and protein immobilization on)
RN 102038-53-9 HCA
CN Carbamic acid, [6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-, 2-(hydroxymethyl)-2-[(1-oxo-2-propenyl)amino]-1,3-propanediyl ester, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 102038-52-8
CMF C29 H41 N5 O14

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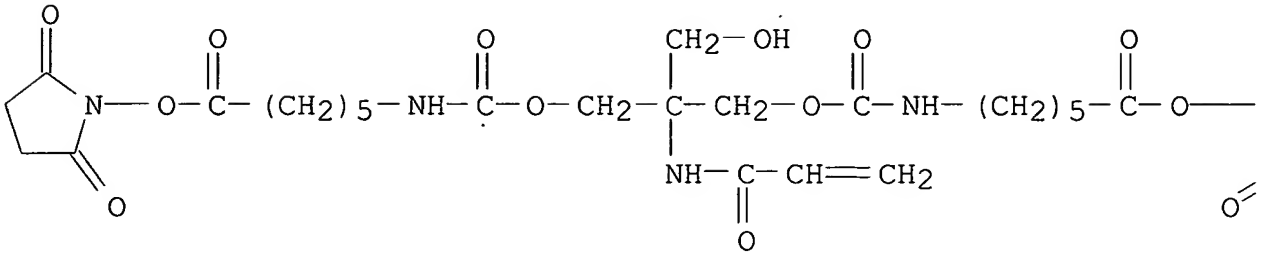
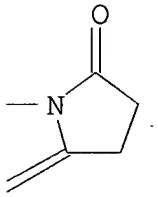


PAGE 1-B



CC 9-3 (Biochemical Methods)
Section cross-reference(s): 7, 15
IT 102038-45-9P 102038-47-1P 102038-51-7P **102038-53-9P**
(preparation and protein immobilization on)

L24 ANSWER 78 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 101:198230 HCA
TITLE: **Polyalkylene glycol**-bound hemoglobins as blood substitutes
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan; Fujirebio, Inc.
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 59104323	A2	19840616	JP 1982-214508	19821207

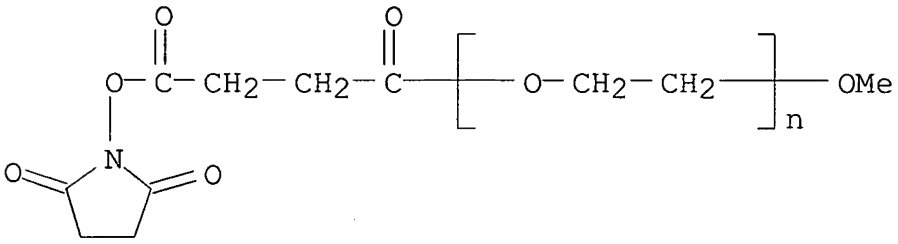
PRIORITY APPLN. INFO.: JP 1982-214508 19821207

AB Blood substitutes are prepared by binding Hb to **polyalkylene glycols** in the absence of O. The Hb may be modified with pyridoxal derivs. prior to binding. Thus, 4 mL 10.9% human Hb solution was dissolved in 18 mL 0.122 M Tris buffer (pH 6.8), and Ar gas was passed through the solution throughout the process. Pyridoxal 5'-phosphate (6.6 mg) was then added, followed by 657 mg monomethoxypolyethylene glycol mono(succimidyl succinate) (average mol. weight 5000). The solution was filtered to obtain 8.2 mL Hb complexes as blood substitutes.

IT **78274-32-5DP**, reaction products with Hb and pyridoxal phosphate
(preparation of, for blood substitutes)

RN 78274-32-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC A61K037-14
ICA A61K031-765
CC 63-7 (Pharmaceuticals)
ST blood substitute Hb **polyalkylene glycol**
IT Hemoglobins
(**polyalkylene glycol** complexes, as blood substitutes)
IT 54-47-7DP, reaction products with Hb and **polyalkylene glycol** derivs. 40225-35-2DP, reaction products with Hb and **polyalkylene glycol** derivs. 42253-87-2DP, reaction products with Hb and **polyalkylene glycol** derivs. **78274-32-5DP**, reaction products with Hb and pyridoxal phosphate 92933-84-1DP, reaction products with Hb and pyridoxal derivs.
(preparation of, for blood substitutes)

L24 ANSWER 79 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 101:157714 HCA
TITLE: Hemoglobin-**polyalkylene glycol**

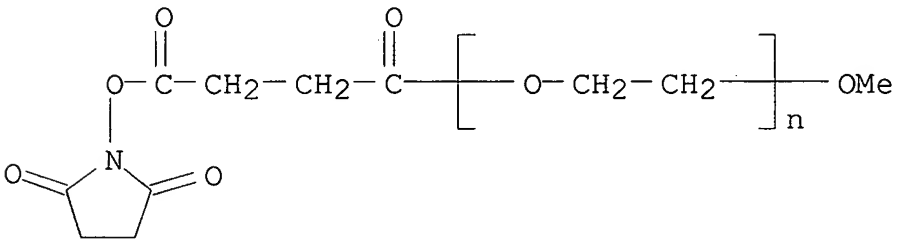
complexes as blood substitutes
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 59089629	A2	19840523	JP 1982-200004	19821115
JP 03059883	B4	19910912		

PRIORITY APPLN. INFO.: JP 1982-200004 19821115

AB Hb and **polyalkylene glycol** are bound with amido groups to form a blood substitute. Hb may be modified with pyridoxal 5'-phosphate, glucose 6-phosphate, or pyridoxal 5'-sulfate. Thus, monomethoxypolyoxyethylene succinic acid monoester [31961-02-1] was treated with N-hydroxysuccinimide [6066-82-6] in the presence of dicyclohexylcarbodiimide in DMF to give monomethoxypolyethylene glycol mono(succimidyl succinate) (I) [**85419-92-7**]. Pyridoxal phosphate-bound Hb was then treated with I to give I-modified Hb.

IT **78274-32-5P**
(preparation of)
RN 78274-32-5 HCA
CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC A61K037-14
ICA A61K031-765
CC 63-7 (Pharmaceuticals)
ST Hb **polyalkylene glycol** blood substitute

IT Blood substitutes and Plasma expanders
(**polyalkylene glycol**-bound Hbs as)
IT Hemoglobins
(**polyalkylene glycol**-bound, as blood substitutes)
IT **78274-32-5P** 85419-91-6P **85419-94-9P**
(preparation of)
IT 54-47-7DP, reaction products with Hb and polyoxyethylene derivs.
78274-32-5DP, reaction products with pyridoxal phosphate-Hb
85419-91-6DP, reaction products with pyridoxal phosphate-Hb
85419-94-9DP, reaction products with Hb
(preparation of, for blood substitutes)

L24 ANSWER 80 OF 81 HCA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 98:166880 HCA
TITLE: Oxygen carrier for blood substitutes
INVENTOR(S): Iwashita, Yuji; Iwasaki, Keiji; Ajisaka, Katsumi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 67029	A2	19821215	EP 1982-302826	19820602
EP 67029	A3	19830803		
EP 67029	B1	19860430		
R: DE, FR, GB				
JP 57206622	A2	19821218	JP 1981-89315	19810610
JP 02006337	B4	19900208		
US 4412989	A	19831101	US 1982-384606	19820603
PRIORITY APPLN. INFO.:			JP 1981-89315 A	19810610

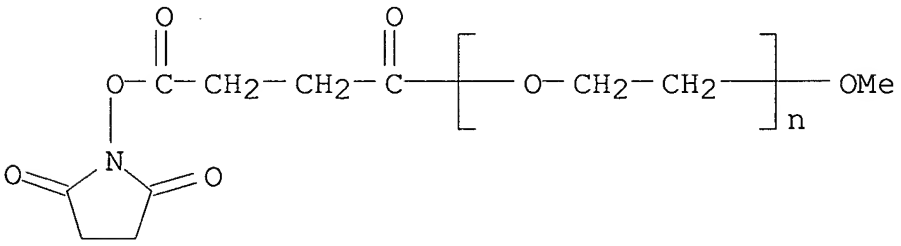
AB An O carrier is **prepared** by introducing at least 1 CO2H group into a **polyalkylene glycol** or polyether and covalently bonding the polymer to an NH2 group of a Hb or a Hb

derivative by amidation. Thus, monomethoxy **polyethylene glycol** succinate [79934-70-6] was stirred overnight at room temperature with N-hydroxysuccinimide in DMF in the presence of dicyclohexylcarbodiimide, the dicyclohexylurea precipitate was separated by filtration, and Et2O was added to the filtrate to obtain monomethoxy **polyethylene glycol** mono(succinimidyl succinate) [**78274-32-5**], which was filtered and added at 0° to a pH 8.5 solution of the pyridoxal 5-phosphate derivative of Hb. The product was purified by ultrafiltration, and freeze-dried to give a modified Hb with a degree of substitution of 6.0 and a mol. weight of 95,000. The half-lives of the Hb-polyether complexes in the circulatory system of rats were 4-7-fold those of Hb, and the complexes showed good ability to deliver O to the tissues.

IT **78274-32-5DP**, reaction products with Hb derivs.
(preparation of, as oxygen carriers for blood substitutes)

RN 78274-32-5 HCA

CN Poly(oxy-1,2-ethanediyl), α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



IC A61K037-14; C08G065-32

CC 63-3 (Pharmaceuticals)

IT 54-47-7DP, Hb derivs., reaction products with polyethers
56-73-5DP, Hb derivs., reaction products with polyethers
1981-49-3DP, Hb derivs., reaction products with polyethers
40225-35-2DP, Hb derivs., reaction products with polyethers
42253-87-2DP, Hb derivs., reaction products with polyethers
78274-32-5DP, reaction products with Hb derivs.
78274-32-5DP, reaction products with Hb derivs.
85419-89-2DP, reaction products with carbonylHbs 85419-90-5DP, reaction products with Hb derivs. 85419-91-6DP, reaction products with Hb derivs. 85419-93-8DP, reaction products with carbonylHb derivs. **85419-94-9DP**, reaction products with Hb derivs.
(preparation of, as oxygen carriers for blood substitutes)

L24 ANSWER 81 OF 81 HCA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 96:149029 HCA

TITLE: Synthetic polymers applied to macroporous silica beads to form new carriers for industrial

affinity chromatography

AUTHOR(S): Schutyser, J.; Buser, T.; Van Olden, D.; Tomas, H.; Van Houdenhoven, F.; Van Dedem, G.
CORPORATE SOURCE: Corp. Res. Dep., Akzo Res., Arnhem, 6800 AB, Neth.

SOURCE: Analytical Chemistry Symposia Series (1982), 9(Affinity Chromatogr. Relat. Tech.), 143-53
CODEN: ACSSDR; ISSN: 0167-6350
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Macroporous SiO2 was coated with crosslinked hydrophilic copolymers, e.g. N-**hydroxysuccinimidyl** 6-acrylamidohexanoate-N-methylolacrylamide copolymer [**81218-36-2**], or N-**hydroxysuccinimidyl** acrylate-N-methylolacrylamide copolymer [81218-37-3], or 6-acrylamidohexanoic acid-N-methylolacrylamide copolymer [81218-38-4] to give carriers suitable for affinity chromatog. The coating process includes adding SiO2 to the functional monomer solution, followed by adding the second monomer (methylolacrylamide), and subjecting the mixture to heterogeneous polymerization in the presence of a radical catalyst. heparin [9005-49-6] And antithrombin III [9000-94-6] were immobilized in one step on these carriers and the resulting conjugates were used to purify antithrombin III and heparin.

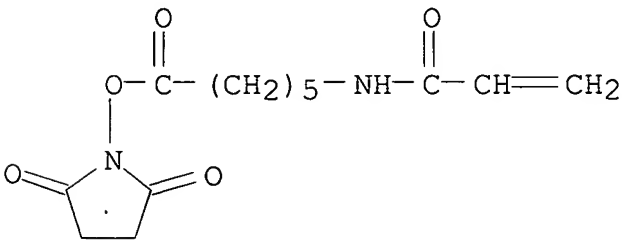
IT **81218-36-2**
(silica coated with, for affinity chromatog.)

RN 81218-36-2 HCA

CN 2-Propenamide, N-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-, polymer with N-(hydroxymethyl)-2-propenamide (9CI) (CA INDEX NAME)

CM 1

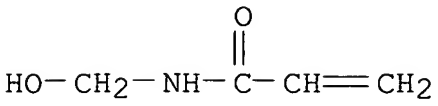
CRN 63392-86-9
CMF C13 H18 N2 O5



CM 2

CRN 924-42-5

CMF C4 H7 N O2



CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 9

IT **81218-36-2** 81218-37-3 81218-38-4
(silica coated with, for affinity chromatog.)

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